THE DIAGNOSIS AND TREATMENT OF ADULTS WITH OBSTRUCTIVE AIRWAYS DISEASE IN GENERAL PRACTICE

by

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CONTENTS

ABSTRACT

This is a study of the diagnosis and treatment of adults with obstructive airways disease in general practice and is in two parts:-

Part 1 - The diagnosis

The aims of this section were to assess, firstly, whether patients diagnosed by their general practitioners as having asthma or chronic bronchitis could be separated by their symptom complexes, secondly, whether the patients' airways reversibility could be predicted from this complex and, thirdly, whether patients with demonstrable airways reversibility were undertreated.

The findings demonstrate that, although patients diagnosed as having asthma or chronic bronchitis could be separated by their symptom complexes, there was considerable overlap between the two groups. In practice differentiation using the symptomatic history would be difficult in about a third of patients. There was a poor correlation between the symptom complex and the bronchodilator and corticosteroid reversibility, though the latter occurred more frequently in those with an asthmatic symptomatology. The majority of patients in whom corticosteroid reversibility was demonstrated had been undertreated.

These findings are of importance to general practitioners in demonstrating that the symptomatic history cannot be used as a reliable basis for diagnosis or to predict airways reversibility. Trials of bronchodilators and corticosteroid therapy are therefore warranted in any patient with troublesome airways obstruction regardless of the symptomatic history.

Part 2 - The treatment

The aim of this section was to undertake a comparative study of the management of patients with obstructive airways disease in several general practices and a specialist clinic and to identify the main problems of drug therapy.

Approximately a fifth of patients seen in general practice had also recently been reviewed by a specialist clinic. Although patients who attended specialist clinics had a similar severity of symptoms to those attending their general practitioners alone, there were noticeable differences in therapy between these groups. Inhaled unlike oral therapy was underused by general practitioners. Prophylactic therapy was underprescribed and underused; compliance with this form of therapy was a major problem. Trials of oral corticosteroid therapy were underused in patients diagnosed as having chronic bronchitis. It is concluded that many patients in general practice receive sub-optimal treatment for their airways obstruction because of a combination of poor compliance and inadequate prescribing.

These findings demonstrate a need to educate general practitioners in the use of appropriate treatment for obstructive airways disease and also to improve the patients' understanding of modern drug therapy.

PREFACE

There are two main problems in the management of obstructive airways disease in general practice, firstly that of making a correct diagnosis and secondly that of giving optimal treatment. In this Thesis these two problems are assessed separately.

The diagnosis-

There is an impression that chronic asthma is often misdiagnosed as chronic bronchitis in general practice, because of the similarity of symptoms in these two conditions. Chronic bronchitis has been associated previously with irreversible and untreatable airways obstruction. A patient given this diagnosis, therefore, may be undertreated. It has been stated that the diagnosis given to the patient is unimportant in clinical practice as the physician usually moves from a symptom complex directly to therapy and provided that adequate treatment is given for reversible airways obstruction, the name attached to the condition is irrelevant (Gross 1980). These statements may be individually true but collectively their validity depends upon the ability to predict airways reversibilty from the symptom complex. Gregg has demonstrated how simple reversibility studies can be undertaken in order to identify those patients who respond to therapy and who are likely to be asthmatic (Gregg 1964). There is little information, however, as to how useful such studies are in the diagnosis and management of patients with airways obstruction in general practice.

The aims of the first part of the survey were to assess:-

1) Whether patients diagnosed by their general practitioners as having asthma or chronic bronchitis could be separated by their symptom complexes.

2) Whether the patients' airways reversibility could be predicted from this complex.

3) Whether patients with demonstrable airways reversibility were undertreated.

The Treatment-

Despite the introduction of efficient bronchodilating and prophylactic drugs there has been little improvement in the death rate from asthma over the past 30 years (OPCS-Mortality statistics). During the same period the hospital admission rate for asthma has almost doubled (OPCS- Hospital inpatient enquiry). Enquiries into the circumstances of asthma deaths have suggested that bronchodilators and corticosteroids were often underprescribed and underused in severe unstable asthma (British Thoracic Society 1982). These findings have been confirmed in studies of new hospital outpatient referrals (Stellman et al 1982). The continuing use of old, potentially addictive, barbiturate containing bronchodilators continues to be a source of concern (Seaton 1978), especially as they are of doubtful efficacy when compared with newer agents (Paterson and Shenfield 1974). Unfortunately some patients find aerosol inhalers difficult to use (Paterson and Crompton 1976), though the magnitude of this problem in the community is unknown. Dry powder inhalers and the spacer device have been developed because of this problem but there is little information as to how often they are used.

A previous study on the treatment of wheezy children in the community suggested an underuse of bronchodilating drugs and that this was probably related to a reluctance to use the diagnostic label- asthma (Speight 1978). Although the need to improve the care

of asthmatics in the community has been realised (Editorial 1981b), there have been few studies concerning this problem in adults. Colmer and Pereira Gray (1983), and Shee et al (1980) have both studied asthma care in single general practices in Exeter and London respectively. The latter group demonstrated the underprescription of effective therapy. However, neither study has given insight into the problems of management in this group of patients, and both studies suffer from the fact that when examining a single general practice individual prescribing habits may become a dominant feature of the study and, therefore, may not be representative of general practice care.

The aims of this part of the survey are:-

1) To study the drug therapy of patients with obstructive airways disease in several general practices.

2) To identify the main problems associated with the use of these drugs and to assess whether such problems are due to inappropriate prescribing or to the patient's misuse of treatment.

3) To compare the management in general practice to that observed in a specialist clinic.

The Thesis is divided into eight chapters. Chapter 1 gives a historical perspective and describes the development of drug therapy for obstructive airways disease. It also gives insight into the difficulties of diagnosis in such patients. Chapter 2 describes the structure of the study and the techniques involved. Chapter 3 includes details of the patients involved. Chapters 4 and 5 describe the symptom complexes and airways reversibility of patients diagnosed by their general practitioners as asthmatic and chronic bronchitic. Chapters 6 and 7 describe the problems associated with the management

of these patients. The last chapter contains the general conclusions of the study.

CHAPTER 1

INTRODUCTION

a) Historical perspectives

b) Modern drug therapy for obstructive airways disease

c) The classification of obstructive airways disease

d) Epidemiology

e) The diagnosis of obstructive airways disease

a) HISTORICAL PERSPECTIVE

-Classical Greek Descriptions

The modern word asthma is derived from the Greek 'ασθμα' meaning "to pant". Though Hippocrates (4th century B.C.) referred to the condition, it was Aretaeus in the 2nd century A.D., who gave the most vivid and surprisingly accurate description (Adams 1856)-

"The symptoms of its approach are heaviness in the chest, sluggishness to one's accustomed work and to every other exertion.... but if the evil gets worse the cheeks are ruddy, eyes protruberant as if from strangulation; a rale during the waking state, but the evil much worse in sleep; voice liquid and without resonance, a desire of much and of cold air."

In contrast his explanation of its aetiology based on a disorder of the spirit or "pneuma" is perplexing to modern ears. Galen believed that the condition was caused by excessive thick secretions draining from the base of the brain on to the lungs. This led Aetius (5th century A.D.) to recommend cautery to the head for the treatment of asthma. In order to thin these secretions Paulus Aegineta in the 7th century A.D. (Adams 1844) recommended the use of attenuent and detergent medicines with:

"continued purging with drastic medicines and vomiting from radishes"

The account of Aegineta suggests that the term asthma may have been used as a description rather than a disease state; this is illustrated in the following passage in which he differentiates asthma from orthopnoea:

"Those who breathe thick without fever, like those who have run fast, are said to be asthmatic, that is to say pant for breath: and from their being obliged to keep their chest erect for fear of being suffocated, they are called orthopnoeic"

-Early English Descriptions

The classical Greek theory of asthma, especially the teachings of Galen dominated medical practice in Europe until the

17th century. This is illustrated by an account of a famous consultation in 1552 between John Hamilton, an influential bishop of St. Andrew's, who suffered from asthma, and Jerome Cardan, Professor of Medicine at Pavia. He attempted to purge the brain by applying ointments to the coronal suture (luckily he also advised the patient not to sleep on a feather bed, and unwittingly cured his patient by antigen avoidance!) (Dana 1921).

Van Helmont in the mid 17th century was the first to dispute the theories of Galen, stating that in asthma:
"nothing rains down from the head to the lungs"
and that:
"remedies are badly applyed to the head in an asthma"
However, his theory of the aetiology of asthma being an imbalance of the body's vital force is as puzzling as that of Galen (Van Helmont 1662).

Thomas Willis was the first to associate asthma with bronchial obstruction (Willis 1679); Sir John Floyer agreed with this basic defect and listed its causes under the titles: air, diet, exercise, and passions. The treatment he advised, however, including emetics, bleeding and blisters, was as uncomfortable as those of ancient Greece (Floyer 1698).

During this period there was a trend to use the term asthma to describe any breathless patient. William Cullen, the famous Edinburgh physician, strongly disapproved of this, stating that the term "asthma" should depend on the presence of particular symptoms and a "particular proximate cause" (Cullen 1784).

Charles Badham was the first to describe chronic bronchitis and, as today, chronic cough and expectoration were the hallmarks of

this condition (Badham 1808). The famous French physician, Laennec, preferred the term "pulmonary catarrh" to bronchitis. He described a condition of "dry pulmonary catarrh" in which attacks of shortness of breath could occur (Laennec 1846). One wonders how he differentiated such patients from asthmatics.

Laennec rightly thought that bronchial narrowing was caused by spasmodic contraction of muscular fibres in the bronchial wall, controlled by nervous stimulation. In 1842 the French physiologist, Longet, demonstrated this innervation by stimulating the Vagus nerve. During this period two substances which could block the actions of this nerve were in use: Belladonna and Datura Stramonium. These were the first specific anti-asthmatic drugs but other medications remained popular. Dobell listed 39 formulations for inhalation and 44 preparations in tablet or powder form (Dobell 1886). Their main constituents were: potassium nitrate, datura stramonium, lobelia, cannabis indica, belladonna, arsenic, potassium iodide, coffee, and tobacco. Henry Hyde Salter admitted that such treatments were "of very irregular and uncertain operation" and that no single successful remedy existed (Hyde Salter 1868).

-Modern Descriptions of Asthma and Chronic Bronchitis

Knowledge of the aetiology of asthma had, however, improved; in 1819 Bostock gave the first account of hayfever and its relationship to asthma. Later Blackley published a classical account of hayfever and hayasthma; relating the symptoms to pollen exposure he designed a method of pollen counting using glycerine on a glass slide (Blackley 1873).

The term "anaphylaxis" was introduced by Richet after noting the change in reaction of dogs to repeated injections of a

preparation of sea anemone (Richet 1908); Von Pirquet used the term allergy for a similar reaction. Asthma was thought to be a phenomenon of anaphylaxis after the discovery that "toxalbumin" of pollen injected into normal subjects had no effect, whereas in asthmatics it could provoke airways obstruction (Meltzer 1910). Modification of clinical reactions by the repeated injection of small quantities of such substances was investigated by Noon and Cooke, and was the basis of desensitization therapy (Noon 1911, Cooke 1918). The term atopy was later used to describe patients who were unusually sensitive to substances in the environment and who had a well defined group of clinical disorders, such as asthma, hayfever, and childhood eczema (Coca and Cooke 1923). This trait was later found to be associated with the capacity to develop antibodies (IgE) to various external substances (or allergens) (Ishizaka and Ishizaka 1971).

Only a proportion of asthmatics, however, were found to have evidence of atopy, and Rackemann classified asthma as extrinsic or intrinsic depending on whether there was evidence of an allergic aetiology or not (Rackemann 1947). He thought that the intrinsic type had a variety of aetiologies from the psychosomatic to infection. Unfortunately the aetiology of non-allergic asthma remains poorly understood.

Surprisingly, it was not until the 1950's that the true impact of smoking on the development of chronic bronchitis and obstructive airways disease was realised (Oswald et al 1953). Later it was demonstrated that the progression of airways obstruction was independent of the severity of cough and expectoration and was the major cause of morbidity (Fletcher et al 1976).

b) MODERN DRUG THERAPY FOR AIRWAYS OBSTRUCTION.

There has been a great change in attitude to the management of airways obstruction in the later part of this century with a greater emphasis on drug therapy. In the 1930's asthma was often considered a psychosomatic disorder and the doctors' attitudes were not always as constructive as they might have been. In the absence of more effective therapy patients were often taught breathing exercises. Children were separated from their families and taught in special schools. Until recently parties of asthmatics were sent to Davos in Switzerland with the help of the British Red Cross (Morrison Smith 1983). It was the development of efficient drug therapy that changed attitudes to the management of asthma.

Bronchodilator drugs

Sympathomimetic Agents-

In 1895 the potent effects of suprarenal gland extracts in man were reported (Oliver and Schafer 1895). Shortly after this the main active principal, adrenaline, was isolated. A group of related amines were later discovered with comparable but not identical physiological actions (Barger and Dale 1910); these substances were called "sympathomimetic".

A dried tablet form of the suprarenal gland was originally used in asthma with some success, however, it was the injectable form of adrenaline that revolutionised the therapy of asthma (especially of the acute attack). Earlier in this century it was often considered the one valuable treatment in asthma (Rackemann 1927).

The development of another sympathomimetic drug called ephedrine occurred at a similar time in the West, though it had been used by the Chinese as a herbal remedy called "Ma Huang" for many

centuries. Ephedrine was first isolated in Japan by Nagai in 1887, and initial clinical studies took place in that country. An oral preparation was later marketed for use in asthma; though it did not achieve instant success probably because initially recommended doses were incorrect.An early therapeutic trial, however, found it of value in over half the patients treated (Leopold and Miller 1927). Herxheimer described the development of tolerance to the bronchodilator effects of ephedrine used over 2-4 days (Herxheimer 1946). This tolerance was overcome by the use of higher doses, but at the risk of inducing side effects such as excitement and urinary retention. Because of these side effects at higher doses, ephedrine in low dose was often combined with theophylline and a barbiturate (the latter drug presumably added to counteract the central nervous system effects). Such combination tablets continue to be used though there is little evidence to support their effectiveness (Paterson and Shenfield 1974).

In 1940 a synthetic sympathomimetic agent was developed and found to be more potent than adrenaline. In Britain it was called isoprenaline. In 1948 Ahlquist introduced a theory that sympathomimetic drugs exerted their effects by actions on two different types of receptors in the body, called α and β receptors (Ahlquist 1948). Unlike adrenaline, isoprenaline was thought to activate only βreceptors and therefore had actions specific to the bronchi, heart and peripheral vasculature. Used by inhalation in therapeutic doses the actions were almost specific to the bronchi. Isoprenaline was unsuccessful when taken orally because of rapid drug metabolism.

In the 1960's other sympathomimetic agents were discovered,

which had selective actions on the bronchi (and peripheral vasculature) with a relative sparing of cardiac effects. Because of the selectivity of these βreceptor actions Lands proposed the theory of having two types of βreceptor: $\beta 1$ and $\beta 2$ with the bronchi having $\beta 2$ receptors (Lands et al 1967). Several drugs with varying degrees of $\beta 2$ rather than $\beta 1$ actions have been developed and are now the mainstay of modern asthma therapy. They include orciprenaline, isoetherine, terbutaline, salbutamol, fenoterol and rimiterol and are usually available in both oral and inhaled forms.

Anticholinergic Agents-

Atropa Belladonna and Datura Stramonium were used in various powders for asthma throughout the 19th century. The chief constituents of these drugs, atropine, was first isolated by Mein in 1832. It has been in regular use both as an injection and as an inhalant since then. As an inhalant, atropine is still occasionally used in combination with adrenaline or isoprenaline, the bronchodilating effects of atropine being slower in onset but more prolonged than the latter two agents. Crompton found that chronic bronchitics were relatively more responsive to atropine than to sypathomimetic drugs; the reverse being true in the asthmatic (Crompton 1968). In 1973 a more selective anticholinergic agent was developed called ipratropium bromide (Poppius and Salorinne 1973). This drug has fewer central anticholinergic effects and has now virtually replaced atropine.

The development of inhaled therapy-

The earliest form of inhaled therapy was from smoke derived from burning various powders and until recently asthma cigarettes were sold "over the counter" at chemists. In 1910 adrenaline was

sprayed directly down a bronchoscope, with benefit in asthma (Graeser 1939). Since that time various atomisers and sprays have been developed to deliver drugs singly, or in combination. Some of the combination solutions for inhalation are still available, such as "Brovon" (containing adrenaline, atropine, and papaverine). Even in 1929 it was noted that inhalation therapy was associated with far fewer side effects than oral or parenteral treatment (Camps 1929). Until the 1950's the equipment used for inhalation, however, was bulky and often fragile and the introduction of small pressurised aerosol inhalers was a major advance.

Unfortunately aerosol inhalers were later implicated as a cause of an epidemic of asthma deaths in the 1960's (Speizer et al 1968). The isoprenaline inhaler was considered by many to be the major culprit as the rise and fall of its sales in the 1960's in England and Wales was mirrored by a similar rise and fall in asthma deaths (Inman and Adelstein 1969). Before 1967 such inhalers were available without prescription and therefore were possibly more open to abuse. However, isoprenaline may not have been the sole cause of excess asthma mortality. Although a similar epidemic of asthma deaths occurred in Australia, these were not as closely related to isoprenaline aerosol sales (Gandevia 1973). A recent review of asthma deaths in this country has suggested that underuse of drug therapy was more common than overuse (British Thoracic Association 1982). It is possible that, following the epidemic of deaths in the 1960's, there may be now underuse of aerosol inhalers in the community because of fear of their untoward effects (Stableforth 1983).

Recently it has become evident that some patients are unable to use aerosol inhalers properly (Paterson and Crompton 1976, Epstein

et al 1979). This has resulted in the development of the dry powder inhaler and spacer devices which may be easier to use efficiently.

The methylxanthines-

For many years the stimulant and diuretic properties of the methylxanthines (theophylline, caffeine and theobromine) have been used as infusions as in tea, coffee and cocoa. In the 19th century strong coffee was often recommended for asthma. Unfortunately theophylline, the most potent bronchodilator of the methylxanthines, caused severe gastric irritation and was unsuitable for parenteral use. In the 1940's a combination of theophylline and ethylene diamine was found to be chemically stable and could be given intravenously; this drug was called aminophylline (Herrman et al 1937). Later oral forms of theophylline were introduced which caused less gastric irritation. Unfortunately, theophyllines have a narrow therapeutic range and there is a wide individual variation in drug metabolism (Turner-Warwick 1957). For maximum benefit, therefore, the dosage has to be manipulated to achieve an optimal drug level. Despite these drawbacks, and their moderate potency when compared with sympathomimetic agents (Palmer et al 1971), theophyllines have become popular recently, probably because of the introduction of slow-release preparations which maintain stable serum levels throughout the day.

Prophylactic drugs

The word prophylactic is derived from the Greek meaning "keep guard before". In medical terminology it refers to preventative therapy. Although some of the antispasmodic bronchodilators may be used in this way, only drugs whose action is primarily preventative will be discussed under this heading.

Corticosteroid drugs-

The discovery of the potent effects of adrenocorticotropic hormone (Bordley et al 1949) and cortisone (Randolph and Rollins 1950) was to fundamentally change the outlook of patients with chronic asthma. There was, however, considerable disagreement as to how these drugs should be used. Initial studies suggested that corticosteroids were of little value as a maintenance therapy in chronic asthma (Medical Research Council 1956). Fortunately, these drugs were not abandoned, and their undoubted benefits were later emphasised (Rees and Williams 1962). The high incidence of side effects with systemic corticosteroids was quickly realised (Editorial 1958) and because of this inhalation therapy was investigated at an early stage. Early studies of inhaled hydrocortisone were disappointing because of the high systemic absorption of the drug with only moderate local effects. In 1971-4 two corticosteroid drugs with high topical activity but with little systemic absorption were introduced in aerosol and, shortly after, in dry powder form for inhalation (Morrow Brown et al 1972). These drugs were beclomethasone diproprionate and betamethasone valerate. Such inhaled corticosteroids have now replaced the need for the systemic form in most asthmatics.

Sodium Cromoglycate-

The discovery of sodium cromoglycate in 1965 opened an entirely new therapeutic avenue in asthma care. Although an oversimplification, it has been labelled a mast cell stabilizing agent with anti-allergic properties. Altounyan discovered the substance whilst investigating khellin, a constituent of an ancient remedy from the eastern Mediterranean countries (Altounyan 1967).

Sodium cromoglycate was prepared in powder form for treatment by inhalation; a specially designed turbine type of inhaler was introduced to deliver the powder (the spinhaler). The drug has been found to be especially useful in paediatric practice (Godfrey 1983a), though beneficial results have been recorded in adult asthma (Bernstein 1981, Northern General Hospital, Brompton Hospital and MRC collaborative trial 1976). Because of the lack of systemic absorption sodium cromoglycate has been found to be an extremely safe drug. A few patients have found the powder spinhaler delivery troublesome, but recently an aerosol inhaler has been introduced which, for some, may be preferable.

c) THE CLASSIFICATION OF OBSTRUCTIVE AIRWAYS DISEASE

The Ciba Guest Symposium (1959) introduced the first major classification of obstructive airways disease. Asthma was defined as an abnormality of function, namely variable airways obstruction, rather than using aetiological or physiological terms:-

"Asthma refers to the condition of subjects with widespread narrowing of the bronchial airways, which changes its severity over short periods of time either spontaneously or under treatment and is not due to cardiovascular disease."

they continued:-

"The clinical characteristics are abnormal breathlessness, which may be paroxysmal or persistent, wheezing, and in most cases relief by bronchodilator drugs (including steroids)."

Alternatively, the Symposium defined chronic bronchitis in symptomatic terms:-

"Chronic bronchitis refers to a condition of subjects with chronic or recurrent excessive mucous secretion in the bronchial tree."

they continued:-

"The diagnostic criterion is clinical, and is chronic or recurrent cough with expectoration."

They defined chronic or recurrent cough as that occurring on most days for at least three months in the year during at least two years. The definition did not, therefore, include airways obstruction which is often the main cause of morbidity in the condition. The large group of patients in whom airways obstruction was the dominant feature and which was unresponsive to bronchodilators were defined as having "Irreversible or Persistent Generalised Obstructive Lung Disease" (Chronic Obstructive Airways or Lung Disease is a similar term in use today).

Emphysema was defined by the pathological presence of dilated airspaces distal to the terminal bronchioles; such a definition implied that a clinical diagnosis could only be speculative. Before this symposium, emphysema was a term frequently used for patients with chronic expectoration (and therefore chronic bronchitis) who became breathless. Though changes of emphysema often co-exist with chronic bronchitis further study in these patients has indicated that dyspnoea may occur without co-existent emphysema (Burrows et al 1966).

In 1965 a further report on the classification of chronic bronchitis was published (Medical Research Council 1965) splitting the condition into three main categories:-

1) Simple chronic bronchitis, implying mucoid sputum expectoration.

2) Chronic mucopurulent bronchitis, implying recurrent bronchial infection.

3) Chronic obstructive bronchitis, where expectoration was combined with persistent widespread narrowing of the intrapulmonary airways causing resistance to airflow.

The pathogenesis of airways obstruction in smokers with chronic expectoration remains poorly understood. However, in patients with this condition the mucous derives mainly from the central airways (from mucous gland hypertrophy), whereas the main site of airflow obstruction appears to be in the peripheral airways (Hogg et al 1968). Epidemiologically it has been shown that the progression of airways obstruction is unrelated to the degree of chronic expectoration or the number of infective exacerbations (Fletcher et al 1976). It would seem logical, therefore, to follow the advice of Fletcher and Pride and abolish the term chronic obstructive bronchitis and only use the term chronic bronchitis to describe simple chronic expectoration (Fletcher and Pride 1984).

What term could be used in its place? Perhaps we are wrong to distinguish such patients from those with asthma. Some workers have propounded the theory that those smokers with chronic cough and expectoration who develop airways obstruction have an underlying "asthmatic predisposition" and, therefore, have a variant of asthma (Orie et al 1961). Because of their country of origin this has become known as the "Dutch hypothesis". Bronchial hyper-reactivity is considered by some workers to be the cardinal abnormality in asthma (Bronchial reactivity is usually assessed by the concentration of histamine or methacholine required to cause a given increase in airways obstruction). In support of the Dutch hypothesis is the finding that smokers with airways obstruction may show increased bronchial reactivity (Taylor et al 1985), and in one prospective study of 34 patients with mild chronic bronchitis there was a correlation between the rate of decline in FEV1 over 5 years and the degree of methacholine reactivity and reversibility to isoprenaline

(Barter and Campbell 1976). Reviewing many studies of bronchial reactivity in chronic bronchitis (defined by chronic cough and expectoration) Fanta and Ingram concluded that in these patients there was a range of reactivity from normal to the hyper-reactivity normally occurring in the young asthmatic (Fanta and Ingram 1981). Unfortunately, it is not clear whether those smokers with airways obstruction who demonstrate bronchial hyper-reactivity also had this feature when asymptomatic in youth. As the degree of response to histamine or methacholine may depend upon the initial airways calibre there is some concern that the increased reactivity may be a consequence rather than a cause of the airways obstruction in smokers (Fanta and Ingram 1981).

The role of allergy in smokers who develop airways obstruction is more controversial. In the large study by Fletcher and co-workers the incidence of allergic features was not increased in those patients who developed airways obstruction (Fletcher et al 1976). However, in a study of a younger cohort of men from the group originally analysed by Fletcher's group an association was found between the rate of decline in FEV1 and presence of allergic features (Connellan et al 1982). Barter and Campbell, in their prospective study of chronic bronchitis, found that those patients who developed airways obstruction were more likely to have sputum eosinophilia (Barter and Campbell 1976).

Although non-specific terms such as chronic obstructive airways (or lung) disease have been criticised as being unhelpful (Scadding 1971), they do describe the abnormality causing the morbidity and mortality. Such terms are now becoming increasingly popular and "chronic obstructive lung disease" is now included in the

most recent "International Classification of Diseases" as used by General Practitioners (World Health Organisation 1978).

The 1959 Ciba Guest Symposium definition of asthma did not include any reference as to the degree of change in airways obstruction required to diagnose asthma, nor the period of time in which this change should take place. The second major problem is how to differentiate quantitatively between patients with asthma (variable or reversible airways obstruction) and those with "Irreversible airways obstruction". Unfortunately there are difficulties with the use of airways reversibility to bronchodilators and corticosteroids as a disease characteristic. The response to these drugs depends upon the type and dose of drug used, and how the response is measured. The problems of reversibility studies will be discussed in detail later in the thesis. As yet there is no agreement as to what degree of airways reversibility is required to diagnose asthma (Porter and Birch 1971).

A further problem in the use of symptoms and airways reversibility in definitions is that these features may change with time. It is well known that an asthmatic may present with episodic airways obstruction but later develop irreversible airways obstruction which is unresponsive to bronchodilators and corticosteroids (Brown et al 1984). This is especially likely to occur in asthma presenting in middle age. Scadding has proposed that previous evidence of variable airways obstruction in such patients justifies a diagnosis of asthma (Scadding 1983). Patients with a history of heavy cigarette smoking often give a long history of chronic cough and expectoration and do not notice impaired exercise tolerance unless they have a chest infection. Only a minority

(between 10-20%) develop symptomatic airways obstruction, and this usually progresses with age (Fletcher et al 1976).

It is likely that those patients with truly "irreversible" airways obstruction have primarily emphysema, as the defect in such cases is in the alveoli rather than in the bronchi. Unfortunately, this is a difficult diagnosis to make in life and a recent review has emphasised the poor correlation between clinical, radiological and physiological changes on the one hand and the pathological changes of emphysema on the other (Flenley and Warren 1980).

d) EPIDEMIOLOGY

Epidemiological surveys of adults with airways obstruction are hampered by diagnostic difficulty between chronic bronchitis and chronic asthma in the middle aged and elderly. Estimates of prevalence vary depending on the definitions used and how the disorder is identified in the survey. Asthma is an intermittent condition and therefore, the use of current prevalence (all patients experiencing the condition at a given time) underestimates the incidence of the disease. Period prevalence (all patients having a history of the condition during a given period) or cumulative prevalence (patients having a history of the condition at sometime in their life) may be more representative of disease frequency, but the addition of historical information leads to inaccuracies, especially when one is dependent upon the patient's memory. Variations in disease prevalence between authors in diverse geographical locations may well be due to difference in study design rather than in disease frequency.

Asthma-

The current prevalence of asthma in adolescents and adults

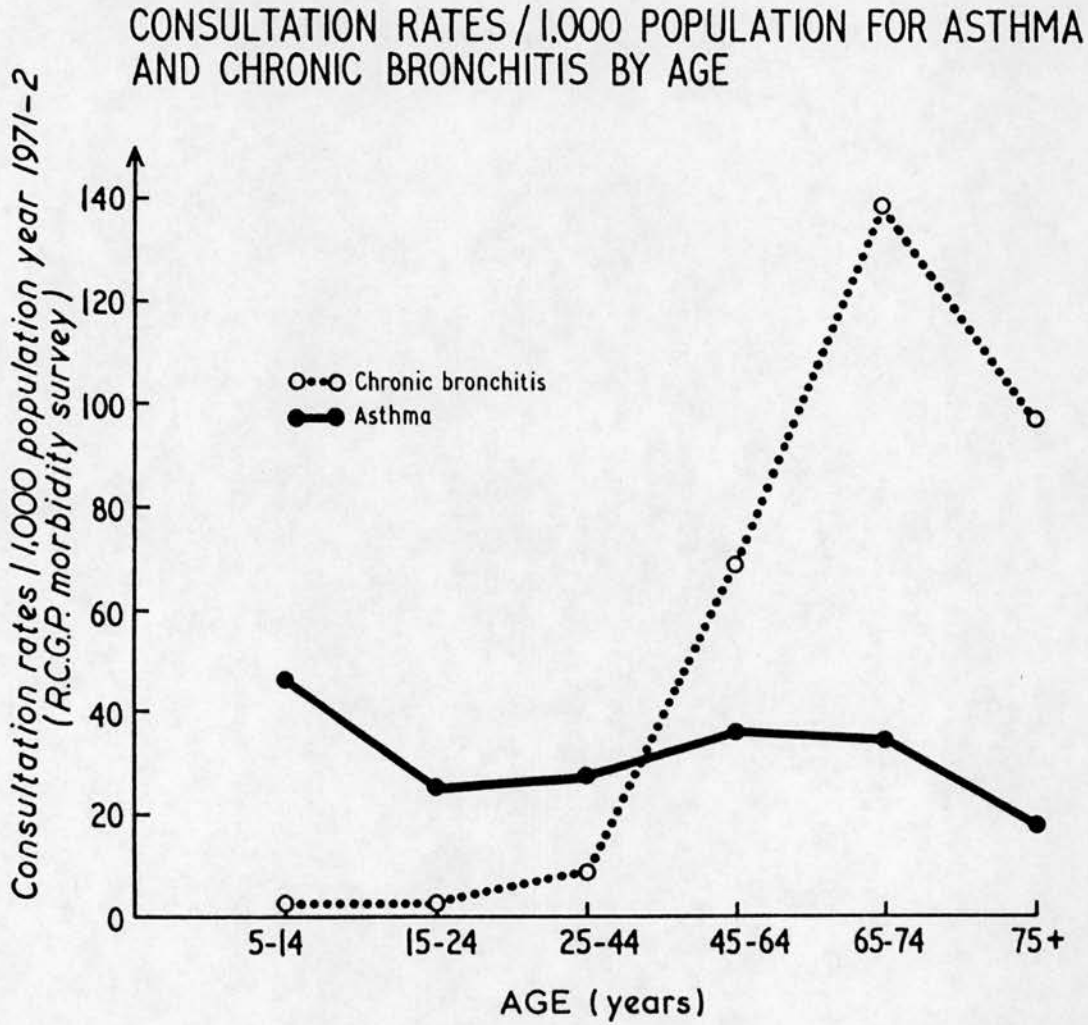
has been reported between 0.9% and 5.4% in several recent surveys. In these studies the male/female ratio has varied between 1.1/1 to 2.8/1.In approximately a half of patients the disease commences below 10 years of age (Gregg 1983a).

Fry estimated that the annual prevalence of asthma in his practice was 1.5%; this prevalence peaked in two agegroups around 10 and 60 years (Fry 1983). Using these figures there would be about 40 asthmatics with ongoing symptoms in an average practice of 2,500 patients. Of these, however, Fry has stated that only a third would attend for treatment in any one year. An assessment of consultation rates (per thousand population) for asthma and chronic bronchitis in England and Wales can be obtained from the General Practice Morbidity Survey 1971-1972 (Royal College of General Practitioners 1979). These consultation rates are illustrated in figure 1.

Chronic Bronchitis-

In the single most useful study of the epidemiology of chronic bronchitis in this country the prevalence was found to be 17% in men and 8% in women for the age group 40-64 years (College of General Practitioners 1961). It is likely that many of these cases were of simple chronic bronchitis without any associated airways obstruction. Using the criterion of chronic cough and expectoration, and breathlessness on the level (when the presence of airways obstruction was likely) the prevalence was lower: 8% in men and 3% in women. The prevalence increased throughout the age range 40-64 years; this being especially marked in males. The male/female ratio rose from 1.2/1 at the age 40-44 years to 2.4/1 at the ages 60-64 years. This is in contrast to a study of chronic bronchitics in chest clinics in which the ratio rose from 1.75/1 at ages 40-49 years to

FIGURE 1


CONSULTATION RATES / 1,000 POPULATION FOR ASTHMA AND CHRONIC BRONCHITIS BY AGE
Consultation rates / 1,000 population year 1971-2 (R.C.G.P. morbidity survey)
140
120
100
80
60
40
20
0
Chronic bronchitis
Asthma
5-14
15-24
25-44
45-64
65-74
75+
AGE (years)

5.2/1 at ages 60-69 years (Medical Research Council 1959). Mortality studies have revealed similar figures to the chest clinic survey suggesting that chronic bronchitis is a more severe condition in males.

Fry estimated that in a general practice of 2,500 with a typical age/sex structure there would be 200-300 patients with chronic bronchitis. However, only about one hundred of these would attend their general practitioner in any one year and 60 of these would have simple chronic bronchitis with no or minimal airways obstruction (Fry 1983). The variation of consultation rate by age as derived by the general practice morbidity survey is illustrated in figure 1.

e) THE DIAGNOSIS OF OBSTRUCTIVE AIRWAYS DISEASE

Clinical history-

In some patients the history is almost diagnostic of asthma; this is especially common in the child or young adult with episodic breathlessness and associated atopic symptoms. In the older patient, however, the history may be less helpful. The following features have been described in teaching texts as being useful in differentiating between asthma and chronic bronchitis (Brewis 1976, Campbell 1984)-

ASTHMA	CHRONIC BRONCHITIS
Nocturnal wheezing attacks	Undisturbed nights
Onset in childhood or adolescence	Onset in middle or old age
Family or personal history of allergy	No history of allergy
Symptoms worse in summer	Symptoms worse in winter
Smoking history uncommon	Smoking history common

There is little information, however, as to how helpful these symptoms are in differentiating between the two conditions. As previously described chronic bronchitis has been defined by chronic cough and expectoration. It is well known that patients with asthma may present with the symptom of cough and occasionally there may be recurrent expectoration (Fletcher 1971). Whether these patients should be described as bronchitic is debatable.

Examination-

Though the presence of wheeze and chest hyperinflation may suggest diffuse airways obstruction, examination of the chest is relatively unhelpful both in differentiating between chronic bronchitis and asthma and assessing the severity of disease (Hetzel and Clark 1983). For this reason no analysis of clinical examination in the diagnosis and assessment of airways obstruction has been undertaken in this survey.

Tests of respiratory function-

In 1846 the first spirometer was used to measure vital capacity (Hutchinson 1846). However, it was not until the 1950's that

the measurement of airways obstruction by the forced expiratory volume in one second (FEV1) and the forced vital capacity (FVC) using a spirometer was widely used. In 1959 details of a portable meter for measuring the peak expiratory flow rate (PEFR) were published (Wright and McKerrow 1959). Whilst the PEFR is more dependent on patient effort than the FEV1, it gives similar information, is easy to perform, and the meter required for its measurement is portable. In short the measurement of the PEFR is ideal for general practice (Gregg 1964). In 1978 a smaller, cheaper PEFR meter (the mini-Wright peak flow meter) was introduced (Wright 1978) and such devices have become increasingly popular.

There are no absolute normal values for FEV1, FVC, and PEFR because these values vary with age, sex and height. Normal ranges of these measurements, taking these variables into account are available (Cotes 1979), and indeed graphs of predicted normal PEFR are provided with each mini-Wright peak flow meter based on a study of normal non-smoking adults in London (Gregg and Nunn 1973). The FEV1, FVC, and PEFR may be recorded, therefore, as absolute values or percentages of the predicted norm. Of course, such norms are means of normal distributions, and in theory measurements are only "abnormal" if they are outside the 95% confidence limits for the normal distribution. Recently the problem of short term variability in FEV1 recordings has been emphasised (Tweeddale et al 1984). Such variability may make the assessment of small changes at low initial values difficult. It is likely that PEFR recordings are similar in this respect.

There is some controversy as to how many "blows" should be made to make a recording of an FEV1 or PEFR. If patients undertake

repeated "blows" during a single period, these measurements have a normal distribution (Ullah et al 1983), suggesting that the use of the mean of several recordings would be scientifically valid. In practice, however, the best of three "blows" is often used (Hughes and Empey 1972) and certainly this method is more suitable for general practice.

It has been shown that most patients are capable of taking their own PEFR recordings at home (Hetzel et al 1979). Such repeated recordings are valuable in the diagnosis of asthma as they may demonstrate variable airways obstruction both spontaneously and as a result of therapy (Prior and Cochrane 1980).

Reversibility studies-

The value of FEV1 and FVC measurements in assessing response to drug therapy was recognised in the 1950's (Hume and Gandevia 1957); such assessments have been called reversibility studies. Similar studies can easily be undertaken in general practice using a peak flow meter (Gregg 1964). Aerosol sympathomimetic agents rapidly reach peak effects. For salbutamol this is approximately 15 minutes after delivery, though about 80% of the response occurs within the first 5 minutes (Tattersfield 1983). Therefore, measurements may be taken before and 10-15 minutes after a dose of such a drug. Usually a standard therapeutic dose from a metered dose inhaler is used, though in some patients a larger response is achieved using higher doses (Prior and Cochrane 1982).

The effects of oral corticosteroids on airways obstruction do not occur for at least 9 hours (Ellul Micallef et al 1974) and the maximal effects may not be apparent for 6-8 days (Shenfield et al 1975, Webb et al 1981a). Because of the suitability of PEFR

recordings for home use, repeated measurements may be undertaken during a course of prednisolone to assess the response. Various other measurements such as the FVC and "the 12 minute walk" may be more sensitive in demonstrating a response to corticosteroids (Williams and McGavin 1980), but these are not easily undertaken in general practice.

At present there are no dose response data for the effects of oral corticosteroids on airways obstruction and the dose used is, therefore, arbitrary. A review of 17 different studies on the effects of corticosteroids on chronic bronchitis illustrates this point; in 10 of these studies prednisolone or prednisone was used in starting doses ranging from 15-60mg daily (Sahn 1978). Low doses of 5mg daily appear to have no effects on patients with chronic airways obstruction (Evans et al 1974). At the present time most workers advise 30-40mg of prednisolone daily to assess corticosteroid responsiveness (Crofton and Douglas 1983).

The expression and interpretation of the reversibility of airways obstruction-

There are a number of ways in which the reversibility of airways obstruction may be expressed:

a) Firstly the change in a measurement after treatment may be expressed in absolute terms. Thus:-

If

Initial measurement = X1

Measurement after treatment = X2

Then

Reversibility = X2-X1

Tweeddale et al found a short term variability in the measurement of

airways obstruction using the FEV1. When this variability was expressed as an absolute change it was independent of the degree of airways obstruction. Because variability expressed as a percentage change would increase with decreasing FEV1, absolute change may be a more reliable as a measure of bronchodilator response (Tweeddale et al 1984). It is likely that measurements of PEFR are similar in this respect.

b) In practice the improvement after treatment is expressed commonly as a percentage of the initial or baseline recording. Put simply:-

Reversibility = 100(X2-X1)/X1%

c) Cotes (1979) has stated that the difference term (X2-X1) is correlated inevitably with the initial value X1. In order to avoid this error he has suggested expressing the improvement as a percentage of the mean of the two values between the measurements before and after treatment.

Thus:-

Change = 2(X2-X1)/(X1+X2)

Reversibility = 100(X2-X1)/$\bar{X}$%

Although this expression may be theoretically correct it is not used commonly in clinical practice.

d) Nicklaus et al have suggested expressing the improvement term (X2-X1) as a percentage of the patient's predicted norm (Nicklaus et al 1969). Thus:-

If

Predicted norm = X3

Then

Reversibility = 100(X2-X1)/X3%

With this expression small changes in a measurement at low initial

values assume less importance, and this may be relevant when there is important short term variation in measurements of airways obstruction as in the FEV1.

Asthma is defined by reversible airways obstruction (either spontaneously or as a result of treatment). No guidelines exist, however, as to the degree of reversibility or variability that constitutes a diagnosis of asthma. Crofton and Douglas (1983) and Crompton (1980) have stated that at least 20% or 25% reversibility (the improvement expressed as a percentage of the initial measurement), respectively, is suggestive of asthma.

CHAPTER 2.

METHODS

a) The practices

b) Patient entry criteria

c) Patient selection

d) The interviews

e) The patient groups

f) The hospital group

g) The questionnaire

h) PEFR recordings and reversibility studies

i) Ethical considerations

j) Computing and statistics

a) THE PRACTICES

Because of the nature of the survey it was not possible to choose the practices at random. The general practitioners were asked to provide the names of patients given therapy for airways obstruction and had to be prepared for the author to undertake interviews of these patients in their premises. Obviously considerable co-operation was required and because of this the practices were selected as those likely to comply with the needs of the study. Of course, the use of random samples of general practitioners would have been preferable but technically difficult to undertake.

Patient management in general practice may be influenced by the local specialist clinic and, therefore, 3 different cities with different available specialist referral centres were chosen.

Five practices were selected, one each in Bradford and Wakefield and three in Leeds. Two practices working from the same health centre and serving a similar population were analysed together because of the small numbers obtained in each practice. Information, therefore, was analysed in four separate practice centres, the details of which are included in table 1.

b) PATIENT ENTRY CRITERIA

1) The patient should be between the ages 16-80 years.

2) The patient should be able to attend his or her general practitioner's surgery.

3) The patient should be currently taking therapy for airways obstruction.

Details of the general practices.

Practice number	1	2	3	4
City	Wakefield	Leeds	Bradford	Leeds
Site	central	central	central	suburb
Number of partners	5	6	3	5
List size	11,200	10,000	6,200	11,000
Does the practice take:-				
Medical students	yes	yes	no	yes
Trainees	yes	yes	no	yes
Does the practice have a diagnostic index.	yes	no	no	no

Table 1

c) PATIENT SELECTION

One of the most efficient ways of identifying patients with a particular disorder in general practice is by the use of a diagnostic index. Unfortunately, only a minority of practices have this facility. In this study one general practice had a diagnostic index and this was used to identify every adult patient taking therapy for airways obstruction in the diagnostic categories asthma and chronic bronchitis during the period January 1981 to June 1981. There was no diagnostic category "Chronic obstructive lung disease" in the classification used (World Health Organisation ICD 1971). No patient had been given a single diagnosis of emphysema.

In the other practices without this facility the general practitioner was asked to record all adults given a prescription (new or repeat) for airways obstruction during an arbitrary two month period (which varied between the practices).

d) THE INTERVIEWS

The practices were visited shortly after the collection of these names and the patients were sent a letter (see Appendix I) asking them to attend their practices for a half hour interview. All interviews were undertaken by the author at times suitable for the patients and the practices, including periods in the early evening and occasionally on Saturday mornings in order to accommodate working men and women. If initial times given to the patient were unsuitable the patient was invited to rebook at a more convenient time. Thankfully practice receptionists were extremely helpful in rebooking appointments. Postal addresses of defaulters were checked but no further follow up of this group was undertaken as it was thought likely that failure to attend or contact the surgery indicated a wish

not to participate in the study.

e) THE PATIENT GROUPS

Patients were split into two main groups depending on their general practitioners' most recent diagnosis. Asthmatics were classed as group A, and chronic bronchitics and all other categories of obstructive airways disease as group B. In nearly all cases the diagnoses were obtained from the patients' records, though if not available it was asked of the patient. Rarely patients were given double diagnoses, for example- asthma and chronic bronchitis. In this case if the term asthma was included at all this was the diagnosis recorded and the patient was classed as group A.

In order to analyse some areas of management, patients in groups A and B were further subdivided into those who had recently attended a specialist clinic (within the previous 12 months) A-OPD and B-OPD, and those who had not A-GP and B-GP.

f) THE HOSPITAL GROUP

In order to compare therapeutic practice in a specialist centre with that of the general practitioners a consecutive series of asthmatics attending a "follow up" specialist clinic were similarly interviewed. This group of patients were classed as group H. Unfortunately not enough patients with chronic bronchitis attended the clinic to form a valid comparison for the general practice group B.

g) THE QUESTIONNAIRE

All interviews were completed between 1/8/1982 and 31/1/1983. A copy of the questionnaire is included in Appendix II. This was designed in a format aiding computerisation of the data with

numerical codes for each answer. The final draft of the questionnaire was produced after trial interviews with in-patient asthmatics. Not all questions were analysed for the report, and some require amplification. The following section includes explanatory notes on the structure of the questionnaire.

Patient number- Each patient was given a three digit code.

Questions 1-3 -Age, sex, and social class.
(Social class was identified as in the Classification of Occupations (Office of Populations, Censuses and Surveys 1970). In the case of minors the father's occupation was recorded).

Question 4 - Are you troubled with wheeze?
(The symptom "wheeze" was often poorly understood by patients. It was amplified to whistling noises on breathing. As nearly all patients answered this question positively it was not used further in the analysis).

Question 5 -How long have you been troubled with wheeze?
(It was obvious from the outset that this question failed to provide sufficient information concerning the age of onset of symptoms. Because of this a further question (5a) was added at the bottom of page 1).

Question 5a -How old were you when your wheeze or shortness of breath became noticeable?
(In this and all subsequent questions concerning wheeze shortness of breath was added as in many patients this feature was by far the dominant symptom).

Is the wheeze (and /or shortness of breath)

Question 6 -Continuous (occurring most days out of the year) or episodic (with symptom free periods)?

Question 7 -Seasonal or perennial?

Question 8 -If seasonal is it most marked in summer or winter?

Question 9-10 -Associated with occupations past or present?

Question 11 -Associated with hobbies?

Question 12 -Associated with animal contact?

Question 13 -Associated with upper respiratory tract infections?

Question 14 -Do/did you suffer from hayfever?

Question 15 -Do/did you have eczema?

Question 16 -Have you a family history of hayfever or eczema?

Question 17 -What time of day is your wheezing worse:- morning, day, evening, night, or no change?

Question 18 -Have you had cough and expectoration most days for at least three months out of the year for the past two years?

Question 19 -Do/did you smoke regularly?
(Regularly was defined as at least daily for a year).

Question 19a -What form of tobacco do/did you smoke mostly:- Cigarettes, pipe or cigars?

Question 20 -How many daily if a cigarette smoker?

Question 21 -Did/does smoking affect your wheeze?:- Better, worse, no change or don't know.

(Questions 6-21 were formulated in order to obtain a symptom history from each patient. The symptoms of patients diagnosed as asthmatic were then compared with those diagnosed as chronic bronchitic).

Question 22 -Have you been warned about smoking by your doctor?

Question 23 -If you have stopped smoking, why?

Have you attended a hospital/chest clinic with your wheeze

Question 24 -As an inpatient?

Question 25 -As an outpatient?

Question 26 -Frequency of inpatient hospital admissions (total)?

Question 27 -Frequency of outpatient attendances (in the past year)?

(Questions 24-27 were designed to ascertain the proportion of patients in general practice who attended specialist clinics. The frequency of inpatient admissions was used as a marker of disease severity. In those chapters dealing with the therapeutic management of the patients, those who had attended a hospital or chest clinic within the previous 12 months were compared with those who had not).

Question 28 - What chest condition do you have? - asthma, chronic bronchitis, emphysema, COAD, don't know.

Question 29 -General Practitioner diagnosis?

Question 30 -Hospital Diagnosis?
(Only the general practitioner's diagnosis was used in this report. The most recently recorded diagnosis was used).

Question 31 -Are you satisfied with your wheeze control?

Question 32 -Is your condition static, deteriorating, or improving?
(These two questions were not used further in this report).

Question 33 -How often have you seen your general practitioner in the past six months?
(This excluded emergency visits).

Question 34 -What is the frequency of emergency house calls made by your general practitioner in the past six months for wheeze?

Question 35 -Have you required injections from your general practitioner in the past six months for wheeze?

Question 36 -How many weeks off school/work have you had in the past year?
(This latter question did not provide sufficient information. If the patient had retired early or received long term sickness benefit because of his/her chest condition this information was added in longhand and analysed separately).

Question 37 -If episodic, how many episodes of wheeze lasting more than one hour have you had in the last month?

Question 38 -If you have morning tightness how long does it normally last?

Question 39 -Do you have more severe wheeze on exercise continuing after the exercise has ceased?
(This question was designed to identify patients with exercise induced asthma. It was stressed that this did not indicate shortness of breath on exertion which quickly improved after rest. The latter could occur with any form of lung disease).

Question 40 -Does this regularly interfere with your activities?

Question 41 -Do you regularly participate in sport?
(This question was not included further in the analysis).

(Questions 31-40 were designed to assess the severity of disease and its control. This information was used in conjunction with symptom scores and peak flow rates to compare severity in groups A,B and H).

DRUG THERAPY

Questions 42-57 -Each patient was asked which drugs he or she was taking or had taken for wheeze.
(Each drug was given a two digit code as shown in Appendix III. Both the drug name and coding were entered on the questionnaire).

Questions 58-61 -Do you take any of the following regularly? Beta blockers, aspirin, antibiotics, cough suppressants, expectorants or antihistamines.
(This information was normally obtained from the patients' records).

Question 62 -Which method of therapy do you prefer? Oral, aerosol inhaler, dry powder inhaler, don't know.

Inhaler use-

Question 63 -Are you using an aerosol inhaler?

Questions 64-65 -Were you shown how to use your inhaler by your general practitioner or by the pharmacist?

Question 66 -Do you think you use the inhaler correctly?

Question 67 -Inhaler technique score- efficient, doubtfully efficient, inefficient?
(This simple assessment was described by Paterson and Crompton (1976))

Questions 68-72 -Inhaler technique- Was the cannister shaken and held upright? Was there co-ordination between activation and inspiration? Was the breath held after inspiration? Was the mouth held open or pursed around the inhaler?

Bronchodilators-

Question 73 -Are/were you using a bronchodilator aerosol inhaler?

Question 74 -(The drug code(s) was/were inserted here).

Question 75 -Is the drug used regularly without regard to wheeze?

Question 76 -Is the drug used on demand?

Question 77 -What is the average daily dose?

Question 78 -Do you use the drug before exercise?

Question 79 -Is it beneficial when used before exercise?

Question 80 -How long does relief from the inhaler last?

Question 81 -How long does an inhaler normally last?

(Questions 79-81 were not used in this report).

Questions 82-84 -Have you noticed the side effects: tremor, palpitations, others?

Questions 85-93 -(These refer to the past use of inhalers and why the drug was stopped).

Questions 94-107 -(These refer to the use of dry powder inhalers and are of a similar format to questions 73-93).

Questions 108-129 -(These refer to the use of oral bronchodilator drugs and again are of similar format to questions 73-93).

Questions 130-133 -(These refer to the use of aminophylline suppositories. These preparations were not used frequently enough to warrant analysis and were not used in this report).

Prophylactic drugs-

Question 134 -Are you using (have you used) sodium cromoglycate?

Question 135 -Do you take the drug regularly without regard to wheeze?

Question 136 -Dose?
(This question refers to the prescribed dose and was obtained from the patients' records if possible.If not recorded it was obtained from the patient).

Question 137 -Are doses missed? Rarely, once per week, once per day or at least twice per day.

Question 138 -Is it used on demand for wheezing attacks?

Question 139 -Is it helpful when used on demand?

Question 140 -Do you use sodium cromoglycate before exercise?

Question 141 -Is it beneficial used in this way?

Question 142 -Does sodium cromoglycate protect against wheeze or treat the wheeze once it is present?

Question 143 -Were you shown how to use the spinhaler?

Question 144 -Do you find the spinhaler technique easier, harder, or the same as an aerosol?

Question 145 -Have you noticed side effects such as coughing or wheezing after sodium cromoglycate?

Question 146 -Was the drug commenced by the patient's general practitioner or a hospital doctor?
(Questions 139, 140, 143 and 144 were not used in this report)

Questions 147-152 -(These refer to the past use of sodium cromoglycate and why the drug was stopped)

Questions 153-167 -(These questions were concerned with the use of inhaled corticosteroids and were of a similar format to those concerning sodium cromoglycate)

Oral corticosteroids-

Question 168 -Are you taking/have you taken oral corticosteroids for wheeze?

Question 169 -Was the drug first prescribed by the general practitioner or a hospital doctor?

Question 170 -How long have you been taking oral corticosteroids?

Question 171 -What dose of oral corticosteroids do you take (in prednisolone equivalent)?

Question 172 -Do you alter your corticosteroid dosage with respect to your wheeze?

Question 173 -Is this on your doctor's recommendation -usually, rarely, always?

Question 174 -By how much do you usually increase your corticosteroid dosage for an exacerbation of wheeze (in prednisolone equivalent)?

Question 175 -For how long do you normally take the raised dose?

Question 176 -When lowering the dose to baseline treatment, do you use a reducing schedule?

Question 177 -Does your wheeze relapse after reducing the dose?

Question 178 -How often do you take raised courses per year?

Questions 179-181 -Have you noticed side effects since commencing corticosteroid therapy? -Weight gain, indigestion, or change in facial appearance. (Other side effects were entered in longhand on the sheet and analysed separately)

Question 182 -If you are not on a corticosteroid inhaler, have you ever been?

Questions 184-191 -(Refer to the past prescription of short courses of oral corticosteroids lasting less than six weeks. They are of a similar format to questions 173-178).

Questions 192-200 -(Refer to the previous use of long courses of oral corticosteroids and why they were stopped).

Questions 201-210 -(Refer to the use of ketotifen.As very few patients used this drug, no analysis of this section was undertaken).

Question 211 -How many courses of antibiotics have you had for your chest in the past year?

Question 212 -Have you had a course of desensitizing injections for your chest?

Question 213 -Do you take expectorants or antihistamines for your chest or have you taken them within the past six months?

Questions 214-216 -(This was the only part of the questionnaire which was completed by the patient, after explanation by the author)

Question 214 -(This was a visual analogue scale assessment and was not used in this report).

Question 215-216 -Please grade your wheeze as an average in the month before interview.

Question 215 -

0. No wheeze -able to do all activities.

1. Slight wheeze -able to do most activities.

2. Moderate wheeze -activities limited regularly by frequent wheeze.

3. Severe wheeze -activities constantly curtailed by wheeze.

Question 216 -

0. No nocturnal wheeze.

1. Slight nocturnal wheeze -woken occasionally, but less than once per week by wheeze.

2. Moderate nocturnal wheeze -woken frequently i.e. 1-3 times per week by wheeze.

3. Severe nocturnal wheeze -woken very frequently i.e. more than 3 times a week with wheeze.

(Questions 215-216 were used to formulate a symptom score. These scores were modified from a published diary card for asthma assessment (Stark 1980)

Questions 217-221 -(These questions were used to record the PEFR recordings and the reversibility studies undertaken with each patient).

h) PEFR RECORDINGS AND REVERSIBILITY STUDIES

All baseline and post-bronchodilator recordings of the PEFR were undertaken using a single mini-Wright peak flow meter. This meter was calibrated by comparing recordings by myself and colleagues against a Wright peak flow meter which itself was maintained and calibrated at the Leeds Chest Clinic.

The best of three PEFR recordings was documented and expressed as a percentage of the patient's predicted PEFR standardised by age, sex, and height (Cotes 1979).

Bronchodilator reversibility-

If the patient's PEFR was below 80% of the predicted value the PEFR recordings were repeated 10 minutes after an inhalation of 200 mcg (2 puffs) of salbutamol via a standard aerosol inhaler. If the inhaler technique had been shown to be inadequate the aerosol was activated by the author.

The level of 80% predicted was chosen for simplicity, but in theory a recording of the PEFR would be "abnormal" only if it was outside two standard deviations from the predicted norm. As two standard deviations is approximately 100L/min (Cotes 1979), it is accepted that some patients with low predicted PEFRs could have values below 80% predicted and still be normal.

Reversibility was expressed, firstly, as the change in PEFR as a percentage of the initial PEFR, and secondly, as the change as a percentage of the predicted PEFR. The first expression was chosen as it is the one most commonly used in clinical practice. However, as mentioned in the introduction, reversibility expressed as the change in PEFR as a percentage of the mean of the initial and post bronchodilator PEFRs may have been scientifically more valid. The second expression of reversibility (the change in PEFR as a percentage of the predicted PEFR) was chosen in order to lessen the impact of small changes at low initial values. This was important in the section of the study comparing patients with asthma and chronic bronchitis, as the latter often had very low initial PEFRs. Analysis of reversibility as expressed by absolute changes in PEFR was not undertaken because this does not take into account the patient's predicted PEFR. For example, if two patients both record PEFRs of 200L/min but one had a predicted PEFR of 400L/min and the other

600L/min, one would not expect both patients to have the same capacity for change.

The results of reversibility were recorded in longhand on the questionnaire and an extra question 219a was added in which the bronchodilator reversibility was expressed by a two digit code.

Corticosteroid reversibility-

If the patient's PEFR was equal to or below 60% of the predicted value he or she was offered a trial of corticosteroid therapy.If accepted the patient was supplied with two identical bottles of tablets labelled A and B. In week one the patient took placebo tablets from bottle A. In week two the patient took prednisolone 5mg tablets, two four times daily (40mg daily) from bottle B. The patient was also taught to use, and was provided with, a mini-Wright peak flow meter and a standard hospital respiratory function chart (see appendix 1V). Patients recorded the best of three peak flow readings morning and evening (not less than four hours after a dose of bronchodilator) throughout the two week period. Each peak flow meter was checked before use by the author measuring his own PEFR. The patient was only aware that he had been prescribed "steroid therapy".

Corticosteroid reversibility was assessed by comparing the mean PEFRs of the last 5 days (10 recordings) during placebo and prednisolone therapy. Only 5 days recordings were used to lessen the possible effects of placebo responses. The change in mean PEFR was expressed as a percentage of the mean inital PEFR during placebo therapy. Paired t tests were also undertaken on the untransformed data for morning and evening recordings separately as some patients

exhibited marked diurnal variation in PEFR.

Patients with a recent exacerbation of symptoms or a history of recent (within the past 6 months) treatment with oral corticosteroids were excluded, as were patients with the following medical complications:- 1) Ischaemic heart disease (current history of angina or previous myocardial infarction), current treatment for congestive cardiac failure or hypertension 2) Diabetes mellitus 3) Known old tuberculosis 4) Indigestion or previous peptic ulcer disease 5) Mental illness 6) Pregnancy 7) Malignancy 8) Inter-current chest infection.

i) ETHICAL CONSIDERATIONS

Full consent was obtained from all patients before interview. Consent was similarly obtained from involved general practitioners and local hospital consultants. The plan of this study was passed by the local medical research ethical committee.

j) COMPUTING AND STATISTICS.

Computing was undertaken using the Statistical Package for Social Sciences (S.P.S.S.) on the AMDAHL computer of the University of Leeds. The data were programmed by Mrs Valerie Binns from the Department of Community Medicine and General Practice, University of Leeds. The majority of data analysis was achieved by question crosstabulation. Not all data were computerised and a small amount of information was correlated by longhand.

Discrete variables were analysed by the chi-squared test, and continuous variables with a non-parametric distribution by the Mann Whitney U test. A linear multivariate analysis (Armitage 1971) was used to assess the value of various symptoms in distinguishing

"asthma" and "chronic bronchitis", as diagnosed by the general practitioner. This latter analysis is discussed in more detail in the appropriate chapter.

CHAPTER 3

PATIENT CHARACTERISTICS

a) Patient attendance rates

b) The diagnostic groups

c) Age and sex distributions

d) Social class distributions

e) A comparison of peak expiratory flow rates and symptom scores between the diagnostic groups

f) A comparison of other markers of disease severity between the diagnostic groups

g) Discussion

a) PATIENT ATTENDANCE RATES

Of the 397 patients requested to participate in the general practice study, 314 attended for interview (79% attendance rate). Table 2 gives an analysis of the insignificant difference in attendance rates between practice centres. In order to assess whether non-attenders were similar to attenders, an analysis of sex (in all practices), age and social class (practice centre 1) of patients in these two groups was undertaken (table 3). No significant difference in these features was found.

b) DIAGNOSTIC GROUPS

201 patients were diagnosed by their general practitioners as being asthmatic and were classified as group A. 107 were diagnosed as having chronic bronchitis and 5 chronic obstructive airways disease; these latter patients were classified as group B (no patient was given a primary diagnosis of emphysema). The number of patients in these two diagnostic groups in each practice centre is shown in table 4. Most patients were obtained from practice centre 1 which had a disease index. In all practice centres except number 2, more asthmatics than bronchitics were obtained.

c) AGE AND SEX DISTRIBUTION

The age and sex distributions of patients in groups A and B are shown in table 5. In group A there were approximately equal numbers of men and women; but there were twice as many men as women in group B. Over a half of group A were below 50 years of age, whereas over 90% of group B were above this age. In group A there were more males than females in those under 30 years of age; this trend was reversed in the 51-70 years age group. There was no

The difference in attendance rates

between the practice centres.

Practice	1	2	3	4	Total
Total number of patients entered	168	89	55	85	397
Number of attenders	140(83%)	62(70%)	45(82%)	67(79%)	314(79%)
Number of non attenders	28(17%)	27(30%)	10(18%)	18(21%)	83(21%)

X^2 6.8 DF3 NS

Table 2.

The difference in sex (all practices),

age and social class (practice centre 1)

between survey attenders and non attenders.

		Attenders	Non attenders
All practices	Sex		
	Male	174(55%)	43(52%)
	Female	140(45%)	40(48%)
	Total	314	83
		X^2 1.3 DF1 NS	
Practice centre 1	Age(years)		
	<30	26(19%)	7(25%)
	30-50	31(22%)	10(36%)
	51-70	56(40%)	10(36%)
	>70	27(19%)	1(3%)
	Total	140	28
		X^2 5.7 DF3 NS	
	Social class		
	I and II	38(27%)	4(14%)
	III	81(58%)	16(57%)
	IV and V	20(14%)	8(28%)
	Total	139*	28
		X^2 4.3 DF2 NS	

* one missing observation

Table 3.

The number of patients in groups

A and B in each practice centre.

Practice	Group A	Group B	Total
1	84	56	140
2	30	32	62
3	33	12	45
4	54	13	67

Table 4.

The age and sex distribution of patients

in groups A and B.

	Group A			Group B		
Sex						
	Male	Female	Total	Male	Female	Total
	99(49%)	102(51%)	201(100%)	75(66%)	38(34%)	113(100%)
Age groups (years)						
<30	37(37%)	23(23%)	60(30%)	0(0%)	1(2%)	1(1%)
30-50	24(24%)	28(27%)	52(26%)	4(5%)	3(8%)	7(6%)
51-70	28(28%)	40(39%)	68(34%)	47(63%)	25(66%)	72(63%)
>70	10(10%)	11(11%)	21(10%)	24(32%)	9(24%)	33(30%)
Total	99(100%)	102(100%)	201(100%)	75(100%)	38(100%)	113(100%)

Table 5.

significant difference in the age of asthmatics between the practice centres (table 6).

d) SOCIAL CLASS

There was a significant difference in social class between groups A and B. Unlike the asthmatics, the chronic bronchitics were predominately from the lower social classes. Table 7 illustrates this distribution and includes the average for England and Wales for comparison. There was a marked difference in social class between the practice centres, varying from 13% to 85% of group A in social classes I and II (see table 8).

The difference in age, sex, and social class distribution between group A and the asthmatics attending a hospital clinic (group H) is illustrated in table 9. Although these patients were of similar age and sex more patients in group H were from the lower social classes.

e) A COMPARISON OF PEAK EXPIRATORY FLOW RATES AND SYMPTOM SCORES BETWEEN THE DIAGNOSTIC GROUPS

Peak expiratory flow rates (PEFR)-

All patients (apart from two who were unable to undertake the manouevre) provided PEFR recordings (the best of three blows being documented). An analysis of the patients' baseline PEFRs expressed as a percentage of the predicted value (Cotes 1979) is included in tables 10, 11 and 12. The asthmatics (group A) had significantly higher PEFRs than the chronic bronchitics (group B) despite differences in age. In patients over 50 years of age the median PEFRs were 60.5% and 44% predicted for groups A and B respectively ($p<0.001$). Younger asthmatics had significantly higher PEFRs than the

The age distribution of asthmatics (group A)

between the practice centres.

	Practice			
	1	2	3	4
Agegroup (years)				
<30	25(30%)	6(20%)	12(36%)	17(31%)
30-50	27(32%)	6(20%)	7(21%)	12(22%)
51-70	22(26%)	16(53%)	12(36%)	18(33%)
>70	10(12%)	2(7%)	2(6%)	7(13%)
Total	84(100%)	30(100%)	33(100%)	54(100%)

X^2 8.8 DF9 NS

Table 6.

The difference in social class between

groups A and B

	Social class				
	I	II	III	IV	V
Group*					
A	28(14%)	56(28%)	95(47%)	16(8%)	5(2%)
B	2(2%)	13(12%)	62(56%)	27(24%)	7(6%)
	X^2 39.3 DF4 p<0.001				
England and Wales	4.8%	19.9%	49%	18.7%	7.6%

*3 missing observations

Table 7.

The difference in the social class of asthmatics (group A) between the practice centres.

	Social class I+II	III	IV+V	Total
Practice				
1	29(35%)	48(57%)	7(8%)	84(100%)
2	4(13%)	16(53%)	10(33%)	30(100%)
3	6(18%)	24(72%)	3(9%)	33(100%)
4	45(85%)	7(13%)	1(2%)	53(100%)

X^2 98.7 DF6 $p<0.001$

1 missing observation

Table 8.

The age, sex, and social class distribution of asthmatics in groups A and H.

	Groups A	H
Age (years)		
<30	60(30%)	11(25%)
30-50	52(26%)	12(25%)
51-70	68(34%)	24(50%)
>70	21(10%)	1(2%)
	X^2 6.2 DF3 NS	
Sex		
Male	99(49%)	25(52%)
Female	102(51%)	23(48%)
Social class		
I+II	84(42%)	11(23%)
III	95(47%)	25(52%)
IV+V	21(10%)	12(23%)
	X^2 9.9 DF4 $p<0.01$	

1 missing observation.

Table 9.

The peak expiratory flow rates (PEFR)(% of the predicted value) of patients in groups A and B.

	Groups	
	A	B
Number of patients	201	111
Median % PEFR (25,75th centiles)	71%(56%,93%)	44%(31%,64%)
	p<0.01	

Table 10.

The difference in peak expiratory flow rates (PEFR) (% of the predicted value) of asthmatics (group A) by age group.

	Age group(years)		
	<30	30-50	>50
Number of patients	60	52	89
Median % PEFR (25th,75th centiles)	83%(67%,96%)	81.5%(60%,96%)	60.5%(39%,74%)
	p=0.62 NS		p<0.001

Table 11.

older; unfortunately not enough young chronic bronchitics were seen to make similar comparisons.

Within group A, patients who had recently attended hospital or chest clinics (within the previous 12 months) - group A-OPD, were compared with those who had attended only their general practitioner -group A-GP. Group A-OPD had significantly lower PEFRs than group A-GP, with group H having an intermediate range of recordings (see table 12).

Symptom scores-

The highest score of 0-3 for day or night time symptoms was recorded for each patient. The distribution of scores for patients in groups A and B are illustrated in table 13. More chronic bronchitics complained of severe symptoms than asthmatics with a third grading their symptoms as severe. However, there was no significant difference in symptom scores between asthmatics in groups H, A-OPD, and A-GP (see table 14). Between 1 in 4 and 1 in 5 patients in these groups graded their symptoms severe.

The relationship between symptom score and PEFR in patients in groups A and B is illustrated in table 15. Of those patients with PEFRs greater than 70% predicted nearly two thirds had scores of 0 or 1 indicating mild symptoms and less than 1 in 10 gave a symptom score grade of 3 indicating severe symptoms: conversely, of those with PEFRs below 50% predicted nearly half gave a score of 3, indicating severe symptoms.

f) A COMPARISON OF OTHER MARKERS OF DISEASE SEVERITY BETWEEN THE DIAGNOSTIC GROUPS

The incidence of several other markers of disease severity was analysed in the different groups including:

The peak expiratory flow rate (PEFR) (% of the predicted value) of patients in groups A-GP, A-OPD, and H.

	Groups		
	A-GP	A-OPD	H
Total number of patients	150	51	48
Median PEFR (%predicted) (25,75th centiles)	74%(50%,93%)	63%(37%,82%)	68%(46%,87%)

*p=0.02
**p=0.16 NS
***p=0.37 NS

Table 12.

The distribution of symptom scores for patients in groups A and B.

Symptom score	Groups A	B
0-1	107(53%)	36(32%)
2	55(27%)	40(35%)
3	39(19%)	37(33%)
Total	201(100%)	113(100%)

X^2 16.5 DF2 p<0.001

Table 13.

The distribution of symptom scores for patients in groups A-GP, A-OPD, and H.

	Groups		
Symptom score	A-OPD	A-GP	H
0-1	27(53%)	80(53%)	26(54%)
2	10(20%)	45(30%)	10(21%)
3	14(27%)	25(17%)	12(25%)
Total	51(100%)	150(100%)	48(100%)

X^2 4.9 DF4 NS

Table 14.

The association between symptom scores and peak expiratory flow rates (PEFR) (% of predicted value)

	Symptom score			
PEFR	0-1	2	3	Total
>70%	78(62%)	35(28%)	12(9%)	125(100%)
50-70%	35(52%)	17(25%)	15(22%)	67(100%)
<50%	30(25%)	42(35%)	48(40%)	120(100%)
Total	143(100%)	94(100%)	75(100%)	312(100%)

X^2 38.6 DF4 $p<0.001$

Table 15.

a) The frequency of emergency housecalls in the previous six months.

b) The number of weeks off work in the previous year.

c) The number of episodes of wheeze lasting longer than one hour in the previous month.

d) The length of morning tightness.

e) The number of previous hospital admissions.

An analysis of these features in groups A and B is included in table 16. Similar numbers of asthmatics and chronic bronchitics had had emergency housecalls in the previous six months, though more asthmatics had had multiple housecalls. The majority of chronic bronchitics were not working, usually because of retirement as most were men. Nearly 1 in 10 received long term sickness benefit, and of the few that did work a half had had a period of at least one week absent from work because of their chest complaint in the previous year.

Approximately 1 in 4 asthmatics had had at least one wheezing attack lasting longer than an hour in the previous month and 1 in 6 had regular morning tightness lasting an hour or longer. About a third of asthmatics and a quarter of the chronic bronchitics had had at least one previous hospital admission in the past.

In order to examine whether patients in groups A-OPD, A-GP, and H were of similar severity the above indices are analysed in table 17. The most marked difference in severity between patients attending hospital clinics (A-OPD and H) and those attending their general practitioner alone (A-GP) was the greater frequency of hospital admissions in the former. Patients in group H also had a greater frequency of emergency housecalls by their general practitioners, though this did not apply to patients in group A-OPD.

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The numbers of patients in groups A and B exhibiting the various indicators of disease severity.

		Groups A	Groups B
Number of patients		201	113
Frequency of emergency house-calls in the previous 6 months.	0	178(89%)	103(91%)
	1	13(6%)	10(9%)
	>1	10(5%)	0(0%)
		X^2 5.2 DF2 NS	
Frequency of weeks off work in the previous year*	0	84(42%)	13(11%)
	1	17(8%)	6(5%)
	>1	28(13%)	5(5%)
	invalided	3(1%)	10(9%)
	not working	69(34%)	79(70%)
Frequency of wheezing attacks lasting >1hr in the previous month*	0	131(65%)	41(36%)
	<5	26(13%)	6(5%)
	>5	25(12%)	4(4%)
	never had wheezing attacks	19(9%)	62(55%)
The length of morning tightness experienced in the previous month	0	80(40%)	37(33%)
	≤1hr	88(43%)	59(29%)
	>1hr	33(16%)	17(15%)
		X^2 2.0 DF2 NS	
Frequency of previous hospital admissions	Never	141(70%)	87(79%)
	1	33(16%)	20(18%)
	2-5	18(9%)	3(3%)
	>5	9(4%)	3(3%)
		X^2 5.5 DF3 NS	

*Comparative statistics not undertaken as not clinically valid.

Table 16.

The number of patients in groups A-GP, A-OPD, and H exhibiting the various indicators of disease severity.

		Groups A-GP	A-OPD	H
Number of patients		150	51	48
Frequency of emergency housecalls in previous 6 months	0	133(89%)	45(88%)	34(71%)
	1	10(7%)	3(6%)	11(23%)
	>1	7(5%)	3(6%)	3(6%)
		X^2 7.3 DF4 NS		
Number of weeks off work in previous year	0	68(45%)	16(31%)	14(29%)
	1	15(10%)	2(4%)	8(17%)
	>1	18(12%)	10(20%)	10(21%)
		X^2 9.2 DF4 NS		
	invalided	2(1%)	1(2%)	0(0%)
	retired	47(31%)	22(43%)	16(33%)
Frequency of wheezing attacks lasting >1hr in previous month	0	99(66%)	32(64%)	28(58%)
	<5	22(15%)	4(8%)	7(15%)
	>5	17(11%)	8(16%)	9(19%)
		X^2 3.4 DF4 NS		
	Never had	12(8%)	6(12%)	4(8%)
Length of morning tightness	0	66(44%)	14(27%)	19(40%)
	<1hr	64(43%)	24(47%)	25(53%)
	>1hr	20(13%)	13(24%)	4(8%)
		X^2 7.6 DF4 NS		
Number of previous hospital admissions	Never	113(75%)	28(55%)	14(29%)
	1	23(15%)	10(20%)	9(19%)
	2-5	11(7%)	7(14%)	15(31%)
	>5	3(2%)	6(12%)	10(21%)
		X^2 47.3 DF6 p <0.001		

Table 17.

Other features of severity were similar in all groups.

g) DISCUSSION.

It was assumed that a representative sample of patients attending their general practitioners with airways obstruction was seen. Although it was not possible to assess the severity and control of disease in the non-attenders, the latter were of similar age, sex and social class to attenders. A response rate of 79% was thought to be satisfactory, especially as patients had been requested to attend their surgeries for an interview with an unknown doctor. Response rates may be higher when interviews take place in the patient's own home by a known doctor (Colmer and Pereira Gray 1983).

By using the prescription of therapy as a selection criterion it is likely that this study is biased towards patients with more severe disease. The proportion of asthmatics and chronic bronchitics studied in relation to the expected number in this general practice population can be approximated from previous epidemiological data. The expected number of asthmatics is:

77% × 38,400 = 29,500
(% of population between 16-80) (practice population)

29,500 × 3%(prevalence of asthma) = 885

(Accepting an asthma prevalence of 3%, and an age distribution of the practice population similar to the average for England and Wales).

As 201 asthmatics were studied this represents a 23% selected sample of the total number expected. Fry (1983), however, in his general practice found an annual prevalence of 1.5% in which case 46% of the expected number of asthmatics in the practice population were seen. He has stated that only a half of a population of adult asthmatics would attend their general practitioner in any one year;

if this is so then nearly all asthmatics expected to attend their general practitioners in a single year in this population were seen. The proportion of asthmatics seen in relation to the number expected varied from 13-32% between the practice centres (using a proposed prevalence of 3%). As expected practice centre 1 using the diagnostic index produced the largest sample.

It is more difficult to assess the proportion of chronic bronchitics seen; this study selected only those with associated airways obstruction and there are few prevalence data on this subgroup. However a comparison can be made with the General Practice Survey (1961). They found a prevalence of chronic bronchitis with breathlessness of 5.5% (average for men and women) in patients 40-64 years old. In this age group we would have expected:

29% (% population aged 40-64 yrs)	×	38,400 (practice population)	=	11,136
11,136	×	5.5% prevalence	=	612

As we analysed 113 patients between 16-80 years it is likely that only 10-15% of cases of chronic bronchitis with airways obstruction were seen.

Asthma is more common in males in childhood and adolescence (Gregg 1983a); this may explain the higher consultation rates of male asthmatics than females under the age of 30 years. There is an impression that late onset asthma is more common in females. Though Gregg has disputed this, stating that there is a tendency to misdiagnose middle aged males as bronchitic rather than asthmatic. Certainly consultation rates are higher in female than male asthmatics over 25 years old (Royal College of General Practitioners OPCS 1979), a fact substantiated by this study. As expected, the

hospital asthmatic group (H) had a similar age and sex distribution as group A. In keeping with previous experience the chronic bronchitics were middle aged or elderly with twice as many males studied as females.

Asthma has been associated traditionally with the upper social classes, though there are few data to support this notion and consultation rates are similar in all social classes (Royal College of General Practitioners OPCS 1979). In this study the asthmatics seen in general practice were biased towards the upper social classes. This is likely to be due to the difference in social class structure of the practices concerned. In contrast the hospital group of asthmatics were of a similar class structure to the national pattern. Chronic bronchitis is a disorder of the lower social classes and in the morbidity survey (Royal College of General Practitioners OPCS 1979) consultation rates in social class V were nearly tenfold those of social class I. The trend towards the lower social classes in this study was present but not as marked, probably because of the higher social class structure of the practices.

Interestingly, there was a variation in the ratio of chronic bronchitics to asthmatics seen in the four practice centres. There are three possible explanations for this. Firstly, if the incidence of chronic bronchitis is increased in the lower social classes, and the incidence of asthma is independent of social class, one would expect the number of chronic bronchitics to increase in relation to those with asthma in practices with more patients from the lower social classes. Unfortunately, without a formal assessment of social class structure in each practice this feature is difficult to examine. However, the centre with the highest ratio of chronic

bronchitics to asthmatics was an inner city practice in an area of high unemployment. Whereas, the practice with the smallest ratio of chronic bronchitics to asthmatics was situated in a wealthy, suburban area of Leeds. In this latter practice 85% of patients seen in the study were from social classes I and II. Secondly, practitioners may be biased in their diagnoses by the social class of the patient, tending to diagnose asthma in patients from the upper social classes and, conversely, chronic bronchitis in patients from the lower social classes. Thirdly, different methods of selecting patients from the practices may alter the number of asthmatics and chronic bronchitics obtained. In practice 1 a diagnostic index was used to identify patients, whereas in the other practices patients were identified by the prescription of therapy. A difference between practice 1 and the others would occur if attendance rates varied between patients with asthma and chronic bronchitis. The use of the diagnostic index was a more efficient way of identifying patients and was less dependent on attendance rate.

Asthma is, by definition, an episodic disorder and the assessment of its severity, therefore, is most accurately undertaken by repeated measurement of lung function (such as the PEFR) and a diary card completed over a period of time (Stark 1980). Such continuous assessment was impractical for this study and yet it was desirable to obtain some objective measurement of the patients' disease severity so that patient groups and their therapy could be compared. By using single recordings of peak flow rates it is accepted that unrepresentative assessments of some patients with episodic symptoms may have been made. The symptom score was adapted from a diary card and was used to grade symptoms over a period of one

month. A single retrospective score was obtained, therefore, rather than multiple prospective assessments as with a diary card. Obviously such a score was subjective and in the author's opinion there was a tendency for patients to underestimate their symptoms.

The section for assessing breathlessness in the MRC questionnaire on respiratory symptoms (a copy is included in Fletcher et al 1976) was considered for inclusion in the author's questionnaire. This being:-

"14a) Are you ever troubled by shortness of breath when hurrying on the level or walking up a slight hill?
14b) Do you get short of breath walking with other people at an ordinary pace on the level?
14c) Do you ever have to stop for breath when walking at your own pace on the level?"

This assessment was thought to be inappropriate for asthma which in many patients is episodic with symptom free periods. However, many asthmatics in the study had continuous symptoms and in retrospect the inclusion of this simple assessment would have been valuable.

In this study the chronic bronchitics were more incapacitated than the asthmatics, with lower peak flow rates and higher symptom scores. The fact that few young chronic bronchitics with mild disease were seen suggests that either such patients do not present to their general practitioners, or if they do are not treated for airways obstruction. It might be expected that asthmatics who attended hospital clinics would have more severe disease than those attending their general practitioners alone. Though the peak flow rates of those attending hospital clinics were slightly lower, these two groups were surprisingly similar in terms of severity of symptoms. The main difference between the two groups was the greater frequency of inpatient treatment in hospital clinic attenders. This may indicate more severe underlying disease in patients attending

hospital clinics, but of course hospital clinic attendance often follows inpatient treatment, and this does not necessarily imply more severe disease.

CHAPTER 4

THE DIAGNOSIS OF OBSTRUCTIVE AIRWAYS DISEASE BY SYMPTOM COMPLEX

a) Univariate analysis

b) Multivariate analysis

c) Discussion

This chapter deals with groups A and B only. It investigates whether patients diagnosed by their general practitioners as asthmatic and chronic bronchitic can be separated by their symptom complexes.

a) UNIVARIATE ANALYSIS

Those symptoms identified from the questionnaire as being potentially helpful in differentiating asthma (group A) and chronic bronchitis (group B) are summarised in figure 2 (the data from which this figure was derived is included in table 18 of the chapter appendix). For simplification 5 patients diagnosed as having chronic obstructive airways disease are included with the 107 diagnosed as chronic bronchitic forming group B. All 5 of these patients fulfilled the M.R.C. criteria for chronic bronchitis (M.R.C. 1965). Because it is likely that differentiation between these two groups would be more difficult in the older patient, a separate analysis of these symptoms in patients over 50 years of age is included in table 18 of the chapter appendix. The symptoms are placed in order according to the level of significance found with the chi-squared test. Figure 3 analyses the incidence of these symptoms in the asthmatics in three different age groups (the full data from which this figure was obtained is included in table 19 of the chapter appendix). Unfortunately not enough young chronic bronchitics were seen to enable a similar analysis to be made.

Some of these symptoms are considered in detail in the following section:-

Chronic cough and expectoration-

This symptom was identified using the M.R.C. criteria for chronic bronchitis (M.R.C. 1965) "Have you had cough and

THE INCIDENCE OF VARIOUS SYMPTOMATIC FEATURES IN ASTHMATICS (GROUP A) AND CHRONIC BRONCHITIS (GROUP B)

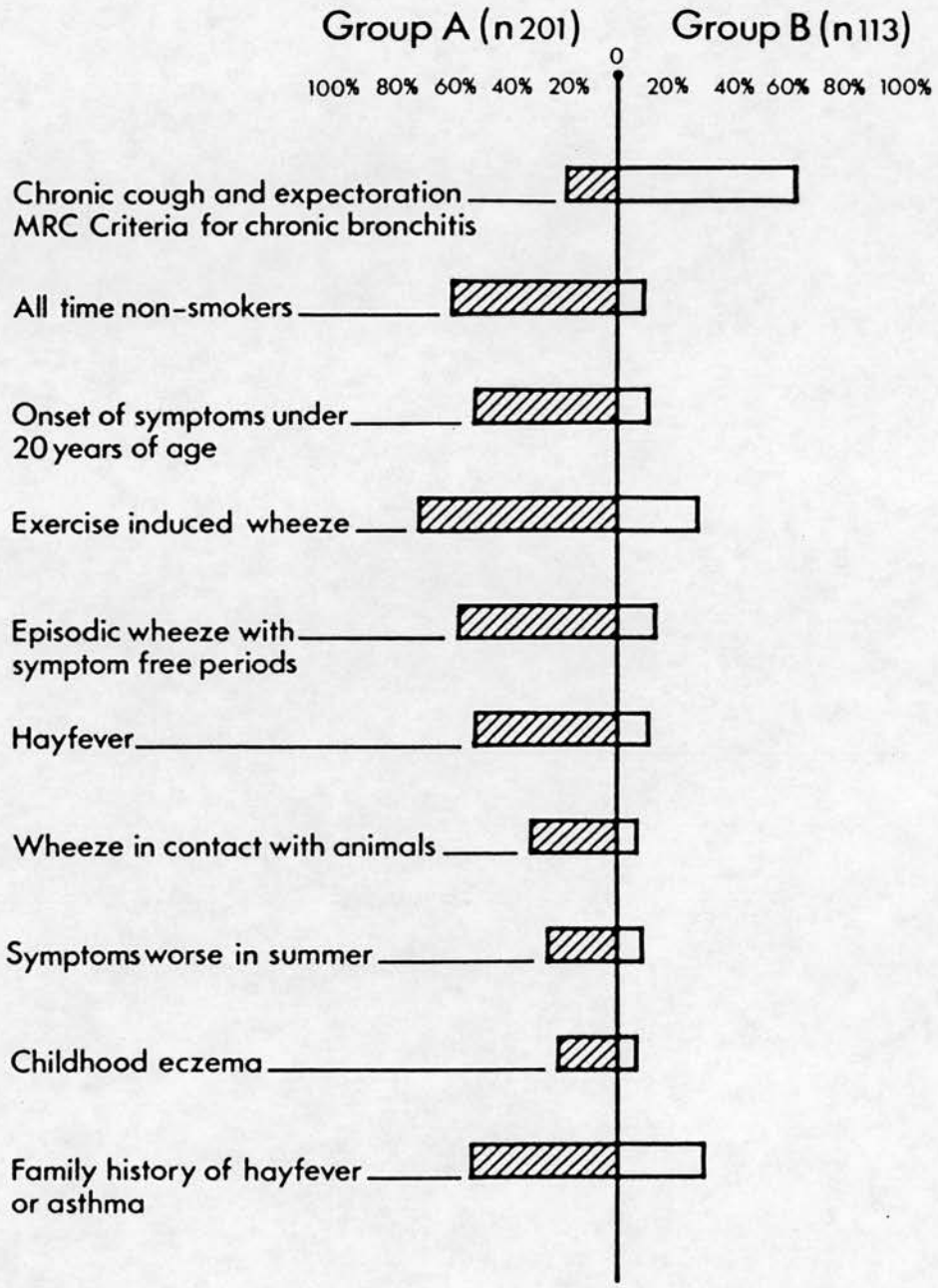


FIGURE 2

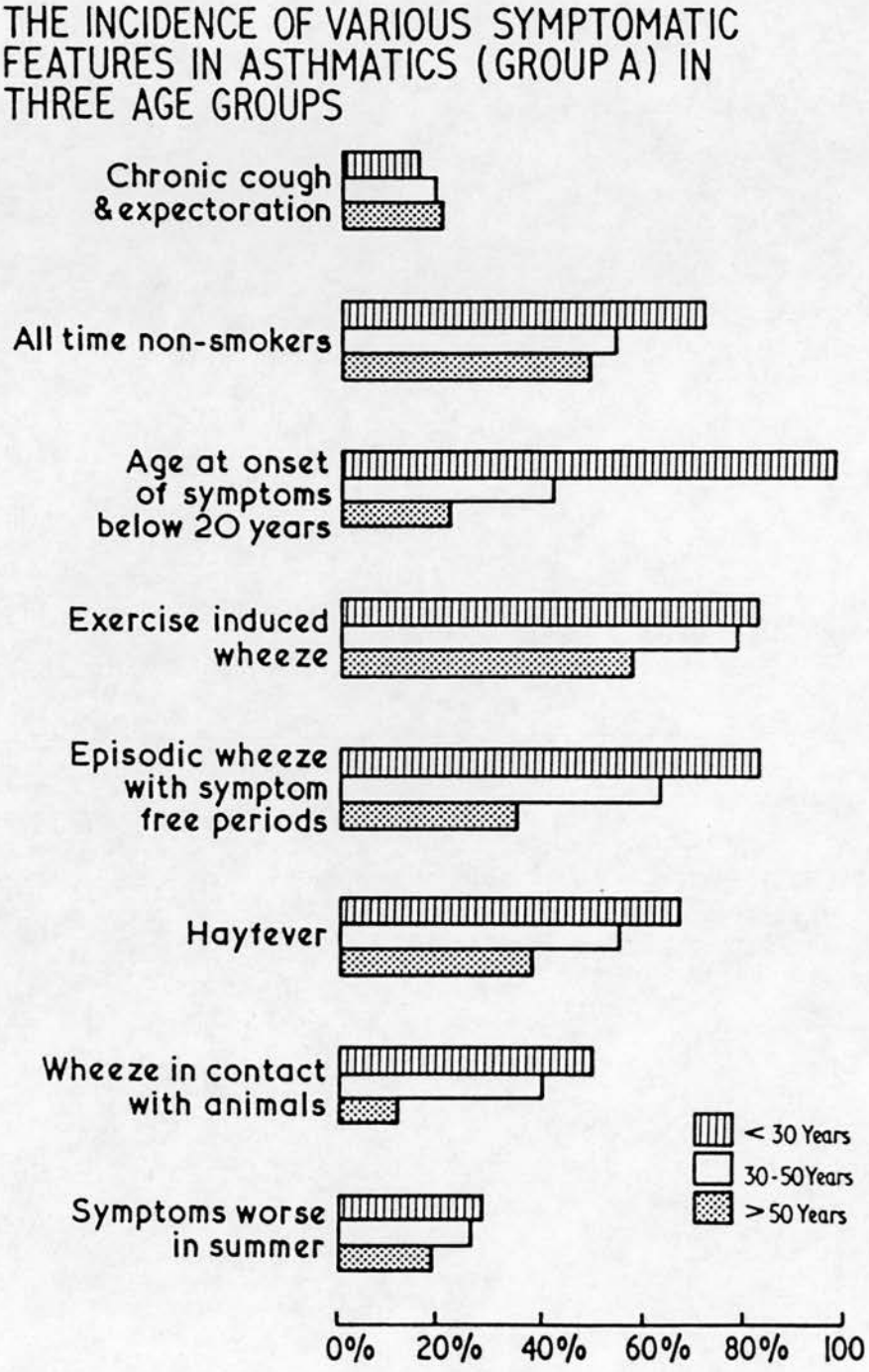

THE INCIDENCE OF VARIOUS SYMPTOMATIC FEATURES IN ASTHMATICS (GROUP A) IN THREE AGE GROUPS
Chronic cough & expectoration
All time non-smokers
Age at onset of symptoms below 20 years
Exercise induced wheeze
Episodic wheeze with symptom free periods
Hayfever
Wheeze in contact with animals
Symptoms worse in summer
< 30 Years
30-50 Years
> 50 Years
0%
20%
40%
60%
80%
100

FIGURE 3.

expectoration most days for at least 3 months out of the year for the past 2 years". A third of those diagnosed by their general practitioners as having chronic bronchitis did not complain of chronic cough and expectoration, whereas a fifth of the asthmatics did (see figure 2). The incidence of this symptom did not vary with age (see figure 3).

Examination of the whole group (A and B) showed that significantly more patients with a smoking history (past or present) gave a history of chronic cough and expectoration (83 out of 185, 45%) than those who were all-time non-smokers (27 out of 129, 20%)(X^2 19.1, DF1, $p<0.001$). However, a similar proportion of asthmatics with a smoking history complained of chronic cough and expectoration (19 out of 86, 22%), as all-time non-smokers (18 out of 115, 16%)($X^2$1.3, DF1, NS).

Smoking history-

A smoking history was defined as having had at least one cigarette daily for at least one year. Only 1 in 8 of the chronic bronchitics were all-time non-smokers in comparison with nearly 6 in 10 asthmatics. The incidence of a smoking history in the asthmatics was similar in all social classes (see table 20).

The effects of smoking on patients airways obstruction was assessed by asking if smoking made their wheeze worse (see table 21). Significantly more asthmatics than chronic bronchitics felt that their wheeze worsened on smoking.

Exercise induced wheeze and episodic rather than continuous symptoms-

Both these features were more common in the younger asthmatics, but even in the over 50 years age group they were still useful differentiating symptoms between the two groups.

The incidence of smoking in group A in the upper and lower social classes

	Social class	
	I&II	III,IV&V
*Number of patients	84	116
Smoker	13(15%)	28(24%)
Non-smoker	52(62%)	62(53%)
Ex-Smoker	19(23%)	26(22%)
	X^2 2.2 DF2 NS	

*1 missing observation

Table 20.

The effect of smoking upon the patients' symptoms in groups A and B.

	Groups	
	A	B
Number of cigarette smokers (current and ex-)	86	99
Number of patients in whom smoking made their wheeze:		
Better	10(12%)	21(21%)
Worse	16(19%)	8(8%)
Unchanged	60(70%)	70(71%)
	X^2 6.3 DF2 $p<0.05$	

Table 21.

Allergic history-

Histories of hayfever, eczema, wheeze in contact with animals, and the presence of asthma or hayfever in a close relative were all more common in the younger asthmatic. Only a history of hayfever was a useful differentiating feature between groups A and B in patients over 50 years old. A history of eczema and wheeze in contact with animals were unusual symptoms in this age group.

Seasonal and diurnal variation of symptoms-

These features were of little value in differentiating between groups A and B. Although more young than old asthmatics had troublesome symptoms in summer, this difference was not statistically significant.

Age of onset of symptoms-

Only a fifth of asthmatics over 50 years of age had an early onset of symptoms (before 20 years of age). This was only a slightly greater proportion than that found in chronic bronchitics (8%).

b) MULTIVARIATE ANALYSIS

The value of various symptoms in discriminating between patients diagnosed by their general practitioners as having asthma or chronic bronchitis has been described using a univariate analysis. Such analysis has the disadvantage of assessing each symptom independently, whereas in reality some of the symptoms (e.g. chronic expectoration and smoking) are likely to be related. If one feature is present, therefore, the other may add little discriminating value. In order to investigate this problem a linear multivariate discriminant analysis using a stepwise process was undertaken (Armitage 1971) using the S.P.S.S. programme (Nie 1975). In this analysis the symptom which most successfully differentiated between

groups A and B was identified and then further factors were added in order of importance, ensuring that each subsequent factor was statistically valuable in the separation of the two groups.

Using the best single factor in discriminating between groups A and B, the presence of chronic cough and expectoration, 81% of group A and 65% of group B were correctly identified (see table 22). The relative risk of being diagnosed as asthmatic given that chronic cough and expectoration was absent was 2.29.

The 11 factors described in table 18 were included in the multivariate analysis. As it was hoped to examine the separation of groups A and B without details of age, sex, or social class, these factors were excluded from the analysis initially. A significance level of 5% was set and this resulted in a discriminant function using 6 factors. In order of importance these were:-

a) Chronic cough and expectoration.

b) Hayfever.

c) Exercise induced wheeze.

d) Episodic or continuous symptoms.

e) An early or late onset of symptoms.

f) Smoking history.

Slight simplification of the numerical coding of the responses in the questionnaire was made for the discriminant analysis, the formulation of which is outlined overleaf:-

Factor	Question	Score
A	Have you had chronic cough and expectoration most days for at least 3 months out of the year in the past 2 years?	1 YES 2 NO
B	Do/did you suffer from hayfever?	1 YES 2 NO
C	Do you have more severe wheeze on exercise continuing after the exercise has ceased?	1 YES 2 NO
D	Is your wheeze or shortness of breath	1 continuous 2 episodic?
E	How old were you when your wheeze or shortness of breath became noticeable?	1 <20 2 20-40 3 >40yrs
F	Do/did you smoke regularly?	0 Smoker 1 Ex-smoker 2 Non-smoker

Discriminant function= 1.22A-0.81B-0.96C+0.66D-0.31E+0.31F+0.03

In comparison with the first 4 factors, the latter 2 added relatively little to the power of discrimination. Using the discriminant function each patient was given a predicted diagnosis. Table 23 illustrates the effectiveness with which groups A and B were separated using the discriminant function; in 83% of the asthmatics and 88% of the chronic bronchitics the predicted and general practitioner diagnoses were matched (relative risk 7.22). The discriminant function can be compared with the use of the best single discriminating factor, chronic cough and expectoration, with which 81% of group A and 65% of group B were identified correctly. A study of the stacked histogram of the discriminant functions of the whole group (figure 4) shows that low values were characteristic of group B

The value of the symptom "chronic cough and expectoration" in differentiating between groups A and B.

Group	No chronic cough and expectoration	Chronic cough and expectoration	Relative risk
A	163(81%)	38(19%)	2.29
B	40(35%)	73(65%)	

Table 22.

The value of the discriminant function in differentiating between groups A and B

Groups	Predicted group A	Predicted group B	Relative risk
A	167(83%)	34(17%)	7.22
B	13(12%)	100(88%)	

Table 23.

The value of the discriminant function when obtained from one half of the patients in groups A and B and applied to the other half.

Groups	Predicted group A	Predicted group B	Relative risk
A	77(76%)	24(24%)	3.55
B	12(21%)	44(79%)	

Table 24.

The value of the discriminant function in differentiating between patients in groups A and B over 50 years old.

Groups	Predicted group A	Predicted group B	Relative risk
A	73(82%)	16(18%)	5.38
B	16(15%)	89(85%)	

Table 25.

STACKED-HISTOGRAM OF THE DISCRIMINANT FUNCTION OF ASTHMATICS (GROUP A) AND CHRONIC BRONCHITICS (GROUP B)

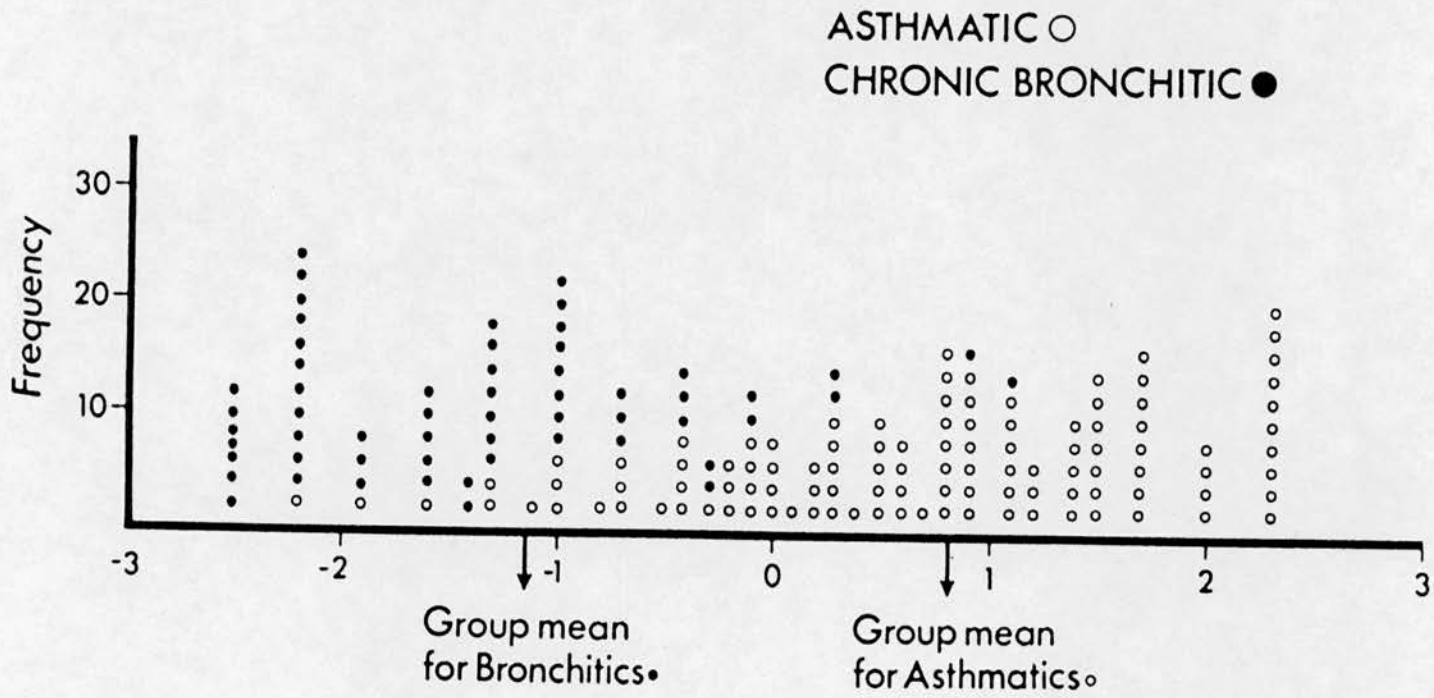


FIGURE 4.

(group mean -1.3), whereas high values were characteristic of group A (group mean 0.73). It is likely that chronic bronchitics with high scores and asthmatics with low scores either had unusual symptoms for the diagnoses or were misdiagnoses.

Using the above function in practice would give less satisfactory results because it was applied to the data in an optimal way to achieve maximal separation of the patients. To investigate the expected loss of accuracy, half of groups A and B (the odd numbered patients) were used to obtain another discriminant function which then was applied to the other half of the data set (the even numbered patients). This discriminant function identified only 4 of the 6 factors previously found to be helpful. These were:-

1) Chronic cough and expectoration.

2) Hayfever.

3) Age of onset of symptoms.

4) Smoking history.

Using the same coding of responses this discriminant function was obtained using the following formula-

Discriminant function= 1.8A-0.8B-0.55E+0.36F-0.94

When this function was used to predict the diagnoses in the other half of the data set, in 76% of asthmatics and 79% of the chronic bronchitics the predicted and general practitioner diagnoses were identical (see table 24). In this case, therefore, separation of the two groups by symptoms was less successful, and this latter analysis is likely to be more representative of its value when used on other groups of patients.

In clinical practice the differentiation of asthma and chronic bronchitis is more difficult in the middle aged and elderly.

Because of this a discriminant analysis was undertaken using only patients over 50 years old (this age limit was chosen arbitrarily).The analysis led to the formulation of another function which identified the following factors-

1) Chronic cough and expectoration.

2) Hayfever.

3) Exercise induced wheeze.

4) Smoking history.

The formula of this function was-

Discriminant function = 1.29A-1.44B-1.01C+0.56F+1.6

82% of the asthmatics and 85% of the chronic bronchitics were given the same predicted diagnoses (see table 25). The separation of these patients can be seen on the stacked histogram illustrated in figure 5.

Other factors were included in a discriminant analysis of the whole group including morning tightness, the effects of smoking on wheeze, bronchodilator reversibility, sex, age, and social class. Only the last two factors were found to be of any additional discriminating value.

c) DISCUSSION.

This analysis suggests that patients diagnosed by their general practitioners as having asthma or chronic bronchitis could be separated by their symptom complexes. These findings are in keeping with a previous community survey of asthma characteristics in wheezing patients (Burr et al 1975), though the latter dealt with an age group in which differentiation between the two groups may have been easier (20-44 years). However, the discriminant analysis provided a mathematical function from symptomatic features to produce

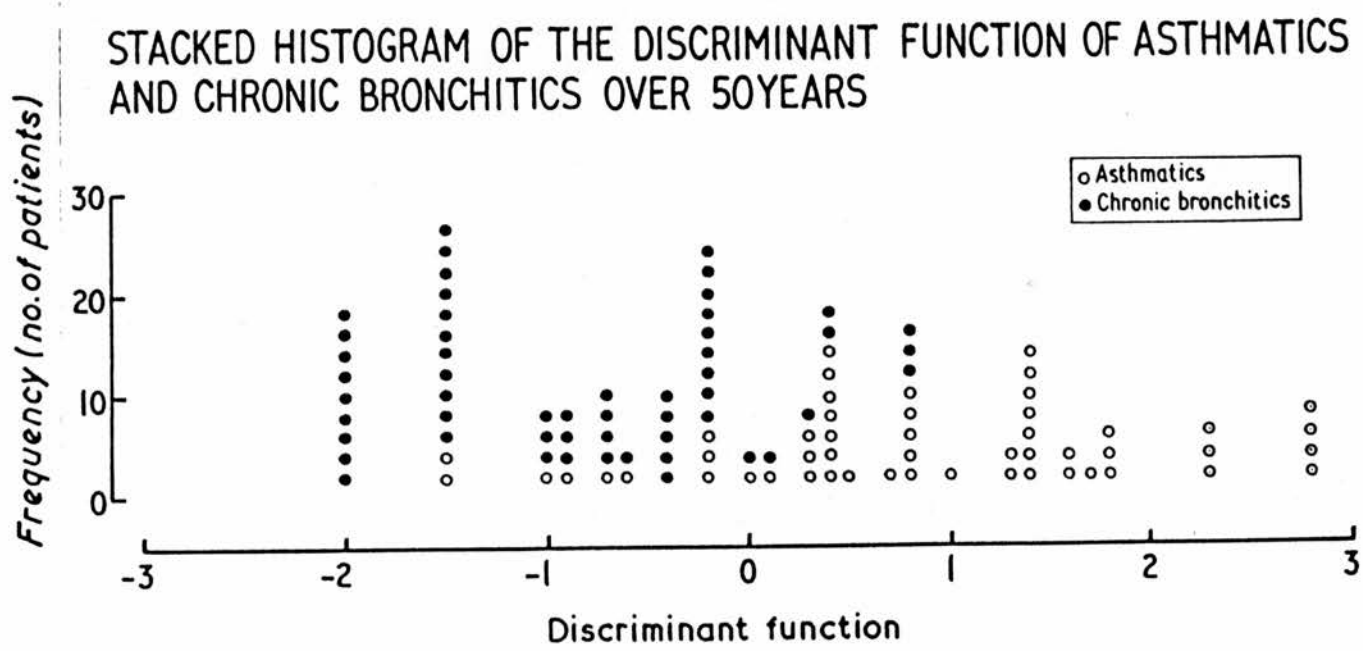

STACKED HISTOGRAM OF THE DISCRIMINANT FUNCTION OF ASTHMATICS AND CHRONIC BRONCHITICS OVER 50YEARS
Asthmatics
Chronic bronchitics
Frequency (no.of patients)
30
20
10
0
-3
-2
-1
0
1
2
3
Discriminant function

FIGURE 5.

maximal separation of the patients with asthma and chronic bronchitis and despite this there was still considerable overlap between the two groups. Observation of the stacked histogram of the discriminant function (figure 4) suggests that in about a third of patients the differentiation between the two conditions using the symptomatic history would be difficult. This group is slightly larger when considering patients over 50 years of age. The difficulties of differentiating asthma from chronic bronchitis in the elderly have been described previously (Burr et al 1979, Lee and Stretton 1972).

In some patients the differentiation between asthma and chronic bronchitis may be artificial as both disorders may co-exist. A fifth of the asthmatics in this study complained of chronic cough and expectoration, fulfilling the criteria for chronic bronchitis (M.R.C. 1965). The incidence of chronic expectoration has been considered greater in older asthmatics (Burr et al 1979, Lee and Stretton 1972), though this study found only a slight increase in this symptom with age. Interestingly, in asthmatics there was no relationship between this symptom and smoking.

The fact that there is a group of patients in whom symptomatic differentiation between asthma and chronic bronchitis is difficult lends support to the Dutch hypothesis. Thus, in any large group of patients with airways obstruction there will be a spectrum of patients. At one end of the spectrum there will be patients with purely asthmatic symptoms and at the other there will be those with symptoms associated with atmospheric pollution (usually cigarette smoking). Between these two poles there will be patients with a mixture of symptoms, perhaps because some of the smokers with chronic expectoration who develop airways obstruction have underlying asthma.

There is controversy about the nomenclature of non-asthmatic airways obstruction (Fletcher and Pride 1984). This study has illustrated the problem well, as the general practitioners use the term chronic bronchitis in a wider sense than the MRC criteria of chronic cough and expectoration (over a third of those diagnosed as chronic bronchitic did not complain of this symptom). In the past it was thought that one could be specific with a clinical diagnosis of chronic bronchitis and emphysema. Dornhorst, in 1956, identified two main types of patients with non-asthmatic chronic airways obstruction and these two clinico-pathological types were later described in detail (Burrows et al 1966). The first type of patient (type A) was considered pathologically to have predominantly emphysema (dilatation of the distal air spaces with wall destruction), and the second type (type B) predominantly chronic bronchitis (mucous gland hypertrophy in the bronchial walls). These two pathological types were thought to have quite well defined clinical profiles. The type A patient had radiological evidence of emphysema, was severely short of breath but maintained normal gas exchange. The patient did not produce much sputum and rarely experienced cor pulmonale. Physiologically the lungs were hyperinflated with an increased total lung capacity and a reduced diffusion coefficient. The type B patient had no radiological evidence of emphysema, usually produced large amounts of sputum and often had a reduced arterial oxygen saturation and hypercapnia. This type of patient was subject to recurrent episodes of cor pulmonale. As mentioned in the introduction, there is now considerable doubt as to the validity of these two clinico-pathological groups (Flenley and Warren 1980). Put simply, many clinicians believe that it is difficult to assess the contribution of emphysema to airways

obstruction in life. Unfortunately therefore, patients with predominant emphysema do not have characteristic symptoms to differentiate them from those with predominant chronic bronchitis and it is impossible to predict how many patients who were labelled as chronic bronchitic by the practitioners in this study were in fact predominantly emphysematous. This is unfortunate as the ability to predict the presence of severe emphysema is clinically important as one would not expect patients with this condition to respond to bronchodilators or corticosteroids.Despite being non-specific, terms such as chronic obstructive airways disease are realistic in that they do not assume a clinical ability to differentiate between chronic bronchitis and emphysema.

The incidence of smoking in the asthmatics (a fifth) was similar to that found in previous outpatient studies (Higenbottam et al 1980, Connolly 1983). In keeping with previous experience (Higenbottam 1980), surprisingly few asthmatics who smoked felt that this made their wheezing worse (a fifth). There is evidence, however, that the rate of decline in the FEV1 is greater in atopic than non-atopic smokers (Connellan et al 1982). It is likely, therefore, that the rate of decline in the FEV1 is greater in smoking asthmatics, and it follows that they should be dissuaded from smoking. The majority of the chronic bronchitics had a smoking history and the relationship between this disorder and smoking is well known (Oswald et al 1953). As expected few chronic bronchitics felt that smoking made their wheezing worse, indeed more felt that it was improved.

Exercise induced asthma has been recognised at least since the 17th century (Floyer 1717). However, only recently has this

reaction been recognised as having diagnostic and therapeutic implications. In the early 1960's it was demonstrated that airways obstruction occurred in young children after 8-12 minutes of exercise and was most severe 1-5 minutes after the exercise (Jones et al 1962). This response was abolished by prior treatment with isoprenaline. Later sodium cromoglycate was found to have a similar protective effect (Godfrey 1983a). The incidence of this reaction in asthmatics depends on the type of exercise involved (Fitch and Morton 1971) and how the airways response is measured. Godfrey (1983b) found that 89% of asthmatic children had a 10% fall in PEFR after exercise. The incidence is probably lower in adults and Poppius et al (1970) found an incidence of 42% in this group (though he used the stricter criterion of a 25% fall in PEFR after exercise). This study substantiates the high incidence of exercise induced wheeze in young asthmatics (83%), however, even in those over 50 years of age a half complained of this symptom. Chronic bronchitics do not develop this response to exercise (Godfrey 1983b) and yet in this study approximately a quarter complained of this symptom. It is possible that some of these patients represented misdiagnoses and were asthmatics. However, the question concerning exercise induced symptoms may not have been specific enough to differentiate accurately between exercise induced airways obstruction and the shortness of breath on exercise which may occur with many forms of lung disease.

Although asthma is defined by the presence of episodic airways obstruction (Ciba Foundation 1957), it is well known that many patients with "late onset asthma" have continuous symptoms (Rackemann 1947), like those with chronic bronchitis. In this study

less than a third of asthmatics over 50 years of age had episodic wheeze with symptom free periods. This factor, therefore, is of less diagnostic value in the older patient.

A history of atopy in a patient with airways obstruction may be a useful indicator that the latter is due to asthma. Skin testing has demonstrated the presence of atopy in 90% of patients whose asthma commenced before the age of 10 years, whereas this applied to only 30% of those whose asthma commenced over the age of 30 years (Pepys 1975). Using the clinical manifestations of atopy (asthma, hayfever and eczema) and skin testing, Pearson (1968) estimated that 55% of asthma in patients aged between 15-29 years was allergic in aetiology; this applied to only 32% of asthmatics aged between 45-60 years. The prevalence of atopic features in asthmatics in this series was entirely compatible with those previous studies. The prevalence of atopic manifestations in the chronic bronchitics was slightly higher than expected. The prevalence of hayfever in the community is approximately 6% (Broder et al 1962) whereas 10% of the chronic bronchitics in this study gave such a history.

Turner-Warwick (1978) has suggested that a family history of asthma is as common in atopic as non-atopic asthmatics, unlike the family histories of hayfever and eczema which are more common in the former. This explains the similar frequency of family history of hayfever and asthma in both older and younger asthmatics. Unfortunately the family histories of hayfever and asthma were not considered separately in this study. Chronic bronchitis is often associated with a strong family history (Oswald 1953). It is possible that the high incidence of family history of hayfever and asthma in this study is related to the misdiagnosis of asthma for chronic

bronchitis in relatives. Consequently the presence of a family history of wheezing chest disorders may be of little diagnostic value. Interestingly Burr et al (1975) found a family history of allergy (asthma, hayfever and eczema) in 24% of their control group when undertaking a survey of asthma characteristics in the community.

Asthma has traditionally been associated with troublesome symptoms at night (Editorial 1983). There is a circadian rhythm of airways calibre in normal individuals, and asthma probably represents an exaggeration of this rhythm, with maximal airways obstruction occurring between 4-6 a.m.(Hetzel and Clark 1980). Asthmatics who have troublesome airways obstruction in the early hours have been called "morning dippers" (Turner-Warwick 1977). This has been estimated to occur in a third of asthmatics (Connolly 1979). In this study approximately a third of asthmatics thought the night to be their most troublesome period. In contrast chronic bronchitics have been found to have little diurnal variation in airways obstruction (Dawkins and Muers 1981) and such patients are thought normally to have restful nights. It was a surprise, therefore, to find that a fifth of the chronic bronchitics thought that the night was their most troublesome period.

The number of patients exhibiting various symptoms in groups A and B -in all patients and in only those over 50 years of age.

Symptom	All patients		Patients >50years	
	Groups		Groups	
	A	B	A	B
Total number of patients	201	113	89	105
Chronic cough and expectoration	37(18%)	73(65%)	18(20%)	66(63%)
	X^2 67.8 DF1		X^2 35.7 DF1	
Smoking history:				
Smoker	41(20%)	37(33%)	15(17%)	34(32%)
All-time non-smoker	115(57%)	14(12%)	44(49%)	13(12%)
Ex-smoker	45(22%)	62(55%)	30(34%)	58(55%)
	X^2 62.0 DF2		X^2 32.0 DF2	
Age at onset of symptoms:				
<20yrs	99(49%)	12(11%)	20(22%)	9(8%)
21-40yrs	51(25%)	31(27%)	24(27%)	27(26%)
>40yrs	42(21%)	65(58%)	41(46%)	67(64%)
	X^2 59.1 DF2		X^2 8.9 DF2	
unknown	9(5%)	5(4%)	5(5%)	2(2%)
Exercise-induced wheeze	143(71%)	30(27%)	52(58%)	25(24%)
	X^2 58.1 DF1		X^2 24.1 DF1	
Episodic wheeze	114(57%)	16(14%)	31(35%)	12(11%)
	X^2 54.0 DF1		X^2 15.3 DF1	
Hayfever	103(51%)	11(10%)	34(38%)	7(7%)
	X^2 53.9 DF1		X^2 28.7 DF1	
Wheeze in contact with animals	62(31%)	7(6%)	11(12%)	7(7%)
	X^2 25.6 DF1		X^2 1.8 DF1	
Symptoms worse in:				
Summer	48(24%)	8(7%)	17(19%)	7(7%)
Winter	56(28%)	45(40%)	23(26%)	41(39%)
Not seasonal	97(48%)	60(53%)	49(55%)	57(54%)
	X^2 15.0 DF2		X^2 8.6 DF2	
Childhood eczema	41(20%)	5(4%)	7(8%)	5(5%)
	X^2 14.8 DF1		X^2 0.8 DF1	
Family history of hayfever/asthma	106(53%)	38(34%)	41(46%)	35(33%)
	X^2 10.6 DF1		X^2 3.3 DF1	
Time of day when symptoms worse				
Morning	70(35%)	53(47%)	33(37%)	47(44%)
night	62(31%)	24(21%)	23(26%)	24(23%
other	69(34%)	36(32%)	33(37%)	34(32%)
	X^2 5.2 DF2		X^2 1.1 DF2	

Table 18.

CHAPTER APPENDIX

The number of patients exhibiting various symptoms in group A in 3 different age groups.

Age group	<30yrs	31-50yrs	>50yrs
Number of patients	60	52	89
Chronic cough and expectoration	9(15%)	10(19%)	18(20%)
	X^2 1.1 DF2 NS		
Smoking history:			
Smoker	12(20%)	14(27%)	15(17%)
non-smoker	43(72%)	28(54%)	44(49%)
Ex-smoker	5(8%)	10(20%)	30(34%)
	X^2 15.5 DF4 p<0.01		
Age at onset of symptoms:			
<20yrs	59(98%)	22(42%)	20(22%)
21-40yrs	1(2%)	28(54%)	24(27%)
>40yrs	0(0%)	1(2%)	41(46%)
Don't know	0(0%)	1(2%)	4(5%)
Exercise induced wheeze	50(83%)	33(63%)	31(35%)
	X^2 12.6 DF2 p<0.01		
Episodic wheeze	50(83%)	33(63%)	31(35%)
	X^2 35.6 DF2 p<0.001		
Hayfever	40(67%)	29(55%)	34(38%)
	X^2 12.2 DF2 p<0.01		
Wheeze in contact with animals	30(50%)	21(40%)	11(12%)
	X^2 26.8 DF2 p<0.001		
Symptoms worse in:			
Summer	17(28%)	14(26%)	17(19%)
winter	17(28%)	16(31%)	23(26%)
not seasonal	26(44%)	22(43%)	49(55%)
	X^2 3.4 DF4 NS		
Childhood eczema	22(36%)	12(23%)	7(8%)
	X^2 18.6 DF2 p<0.001		
Family history of hayfever/asthma	36(60%)	29(56%)	41(46%)
	X^2 3.0 DF2 NS		
Time of day when symptoms worse:			
morning	22(37%)	15(29%)	33(37%)
night	20(33%)	19(37%)	23(26%)
other	18(30%)	18(34%)	33(37%)
	X^2 2.5 DF4 NS		

Table 19

CHAPTER 5

REVERSIBILITY STUDIES IN THE DIAGNOSIS OF OBSTRUCTIVE AIRWAYS DISEASE.

a) Bronchodilator reversibility studies

b) Corticosteroid reversibility studies

c) The treatment of patients with documented reversibility

d) Discussion.

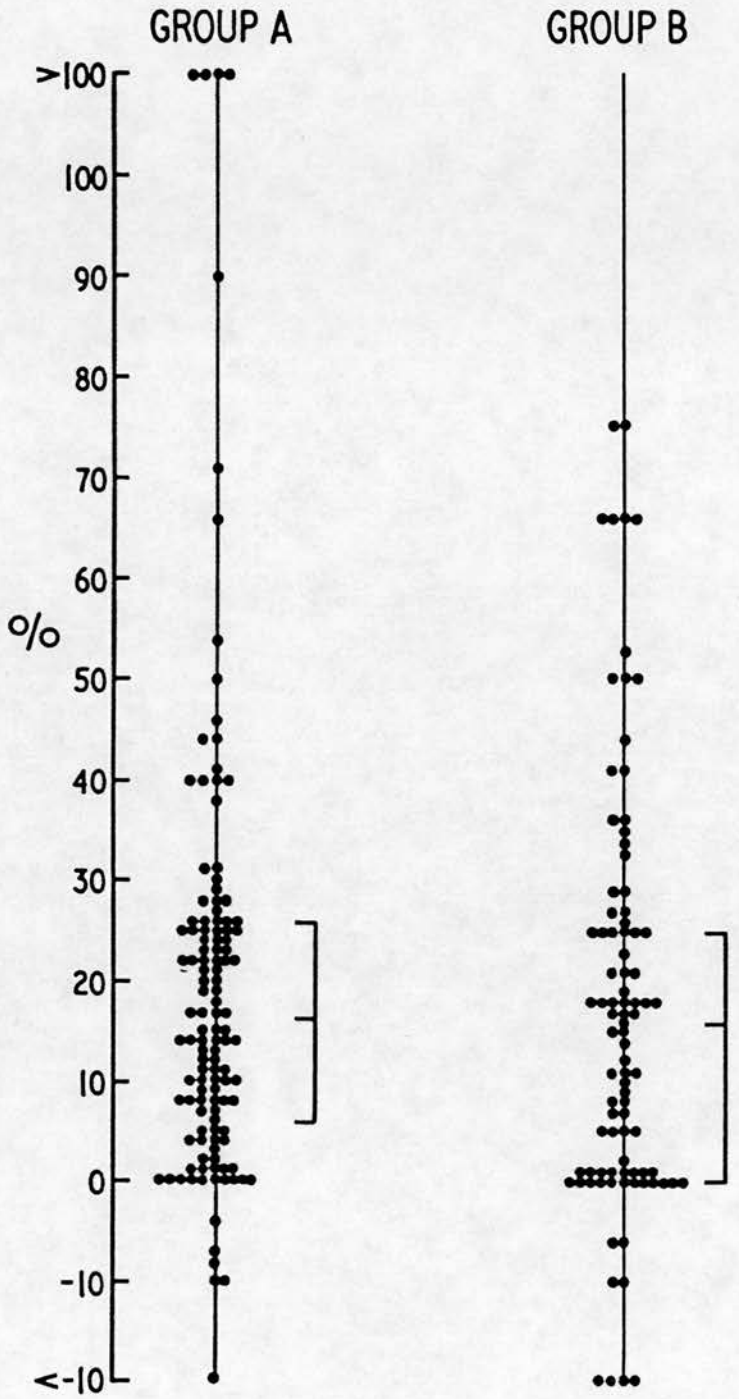
a) BRONCHODILATOR REVERSIBILITY STUDIES

PEFR recordings were undertaken before and 10 minutes after 200 mcg of salbutamol delivered by aerosol in 120 asthmatics (group A) and 95 chronic bronchitics (group B) (all patients with a baseline PEFR below 80% of the predicted value). Bronchodilator reversibility was expressed as the change in PEFR both as a percentage of the initial value and of the predicted value for that patient. The distributions of bronchodilator reversibility expressed in these two ways are illustrated in figures 6 and 7. There was no significant difference in reversibility between the asthmatics and chronic bronchitics when the change in PEFR was expressed as a percentage of the initial value. When this change was expressed as a percentage of the predicted PEFR the difference between the asthmatics and chronic bronchitics was significant, but examination of the distribution (see figure 7) shows considerable overlap and only values over 20% were specific for asthma. This occurred in 16(13%) asthmatics.

Figure 8 illustrates the relationship between the baseline and post bronchodilator PEFR. Only a few patients with mild airways obstruction (>60% predicted PEFR) reached their predicted values with a bronchodilator, and there was no obvious relationship between response and the degree of initial impairment. Neither was there a significant difference in reversibility between older and younger asthmatics (see table 26).

In the previous chapter each patient was given a predicted diagnosis using a discriminant function equation. Using this function more negative values were characteristic of group B and positive values of group A. Figure 9 illustrates the relationship between bronchodilator reversibility (the change in PEFR being expressed as a

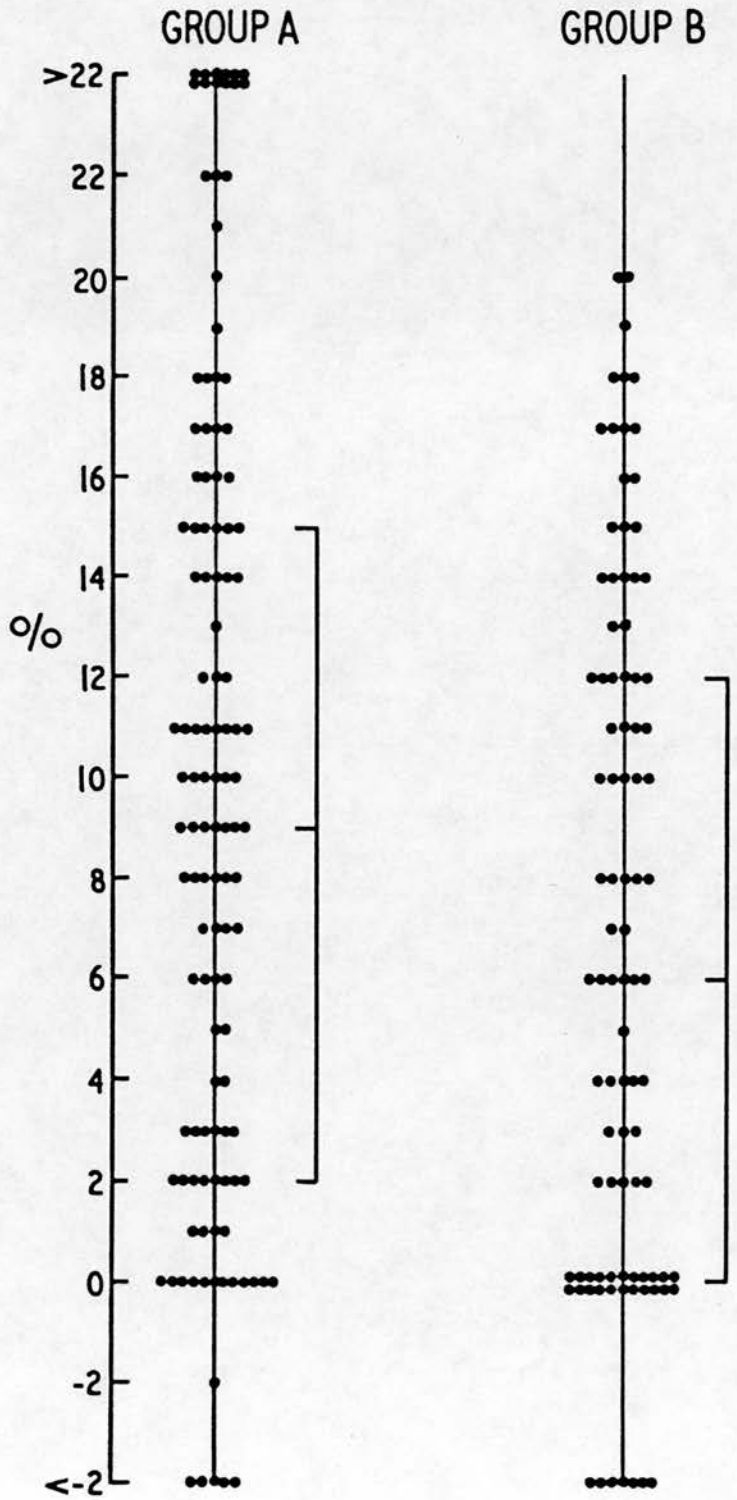
BRONCHODILATOR REVERSIBILITY (THE CHANGE IN PEFR EXPRESSED AS A PERCENTAGE OF THE INITIAL VALUE) IN ASTHMATICS (GROUP A) AND CHRONIC BRONCHITIS (GROUP B).



] = Median (25th, 75th centiles)

FIGURE 6.

BRONCHODILATOR REVERSIBILITY (THE CHANGE IN PEFR EXPRESSED AS A PERCENTAGE OF THE PREDICTED NORM) IN ASTHMATICS (GROUP A) AND CHRONIC BRONCHITICS (GROUP B)



} = Median (25th, 75th centiles)

FIGURE 7

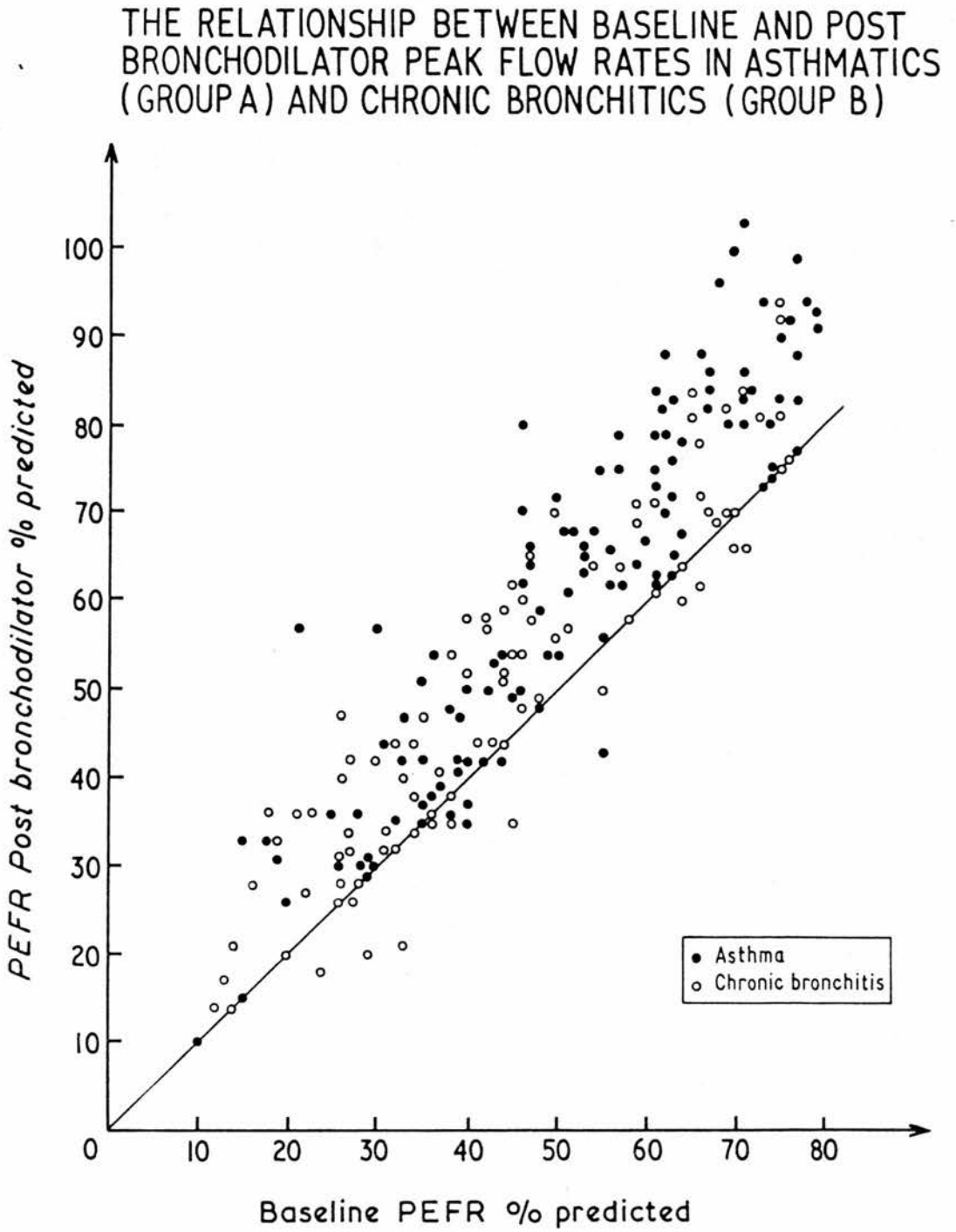

THE RELATIONSHIP BETWEEN BASELINE AND POST BRONCHODILATOR PEAK FLOW RATES IN ASTHMATICS (GROUP A) AND CHRONIC BRONCHITICS (GROUP B)
PEFR Post bronchodilator % predicted
Baseline PEFR % predicted
0
10
20
30
40
50
60
70
80
90
100
Asthma
Chronic bronchitis

Figure 8

The median (25,75th centiles) bronchodilator reversibility (change in the PEFR expressed as a percentage of the predicted norm) in groups A and B in two agegroups.

	Median (25th,75th centile) reversibility. (n=number of patients involved)	
	Groups	
	A	B
Total patients	9%(2%,15%) ** n=120	6%(0%,12%) n=95
≤50yrs	10%(2%,16%) n=49	12%* n=4
>50yrs	8.5%(1%,18%) n=71	**6%(0%,14%) n=91

*Number too small for comparative statistics

**$p<0.05$ Mann-Whitney U test

Table 26.

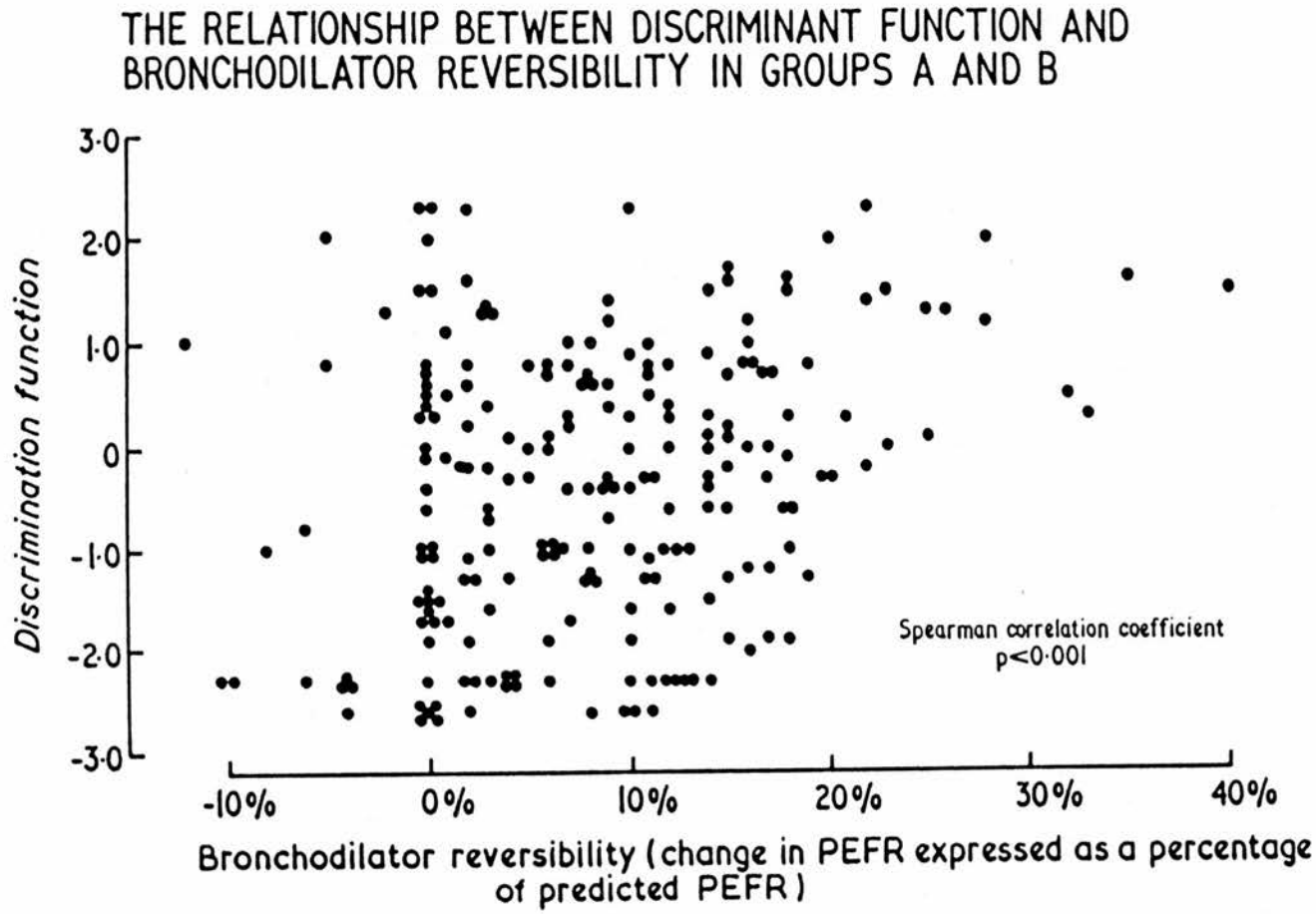

THE RELATIONSHIP BETWEEN DISCRIMINANT FUNCTION AND BRONCHODILATOR REVERSIBILITY IN GROUPS A AND B
Discrimination function
3·0
2·0
1·0
0
-1·0
-2·0
-3·0
Spearman correlation coefficient
p<0·001
-10%
0%
10%
20%
30%
40%
Bronchodilator reversibility (change in PEFR expressed as a percentage of predicted PEFR)

FIGURE 9

percentage of the predicted value for each patient) and the discriminant function. Although this correlation was significant (Spearman's test $p<0.001$) examination of the plot reveals a wide scatter and only a reversibility greater than 20% was specific for a discriminant function "predicted" diagnosis of asthma.

An arbitrary level of bronchodilator reversibility was chosen and those with values equal to or above 10% were compared with those below 10% (change in PEFR as a percentage of the predicted value). The characteristics and symptoms of patients in these two groups are illustrated in figure 10 (the data from which this figure is derived are included in table 27 of the chapter appendix). Of those who had good reversibility ($\geq$10%) significantly more were non-smokers, had episodic symptoms, troublesome nocturnal wheeze and were female. However, observation of figure 10 suggests that none of these differences was great enough to be clinically valuable. A discriminant analysis was undertaken between those with poor (<10%) and those with good reversibility ($\geq$10%) using the same features described in the previous chapter (but including age and sex). Only sex, and the season and time of day in which the symptoms were most severe were of discriminating value. Using this discriminant function less than two-thirds of patients were grouped correctly by reversibility (see table 28). Observation of the stacked histogram of this discriminant function in figure 11 emphasises the poor separation of patients.

50% of group A and 39% of group B had reversibilities of 10% or greater. Table 29 illustrates that the discriminant function did not help in predicting "good" bronchodilator reversibility.

The incidence of various factors in patients with bronchodilator reversibility (the change in PEFR expressed as a percentage of the predicted norm) equal to or above 10%, or below 10%

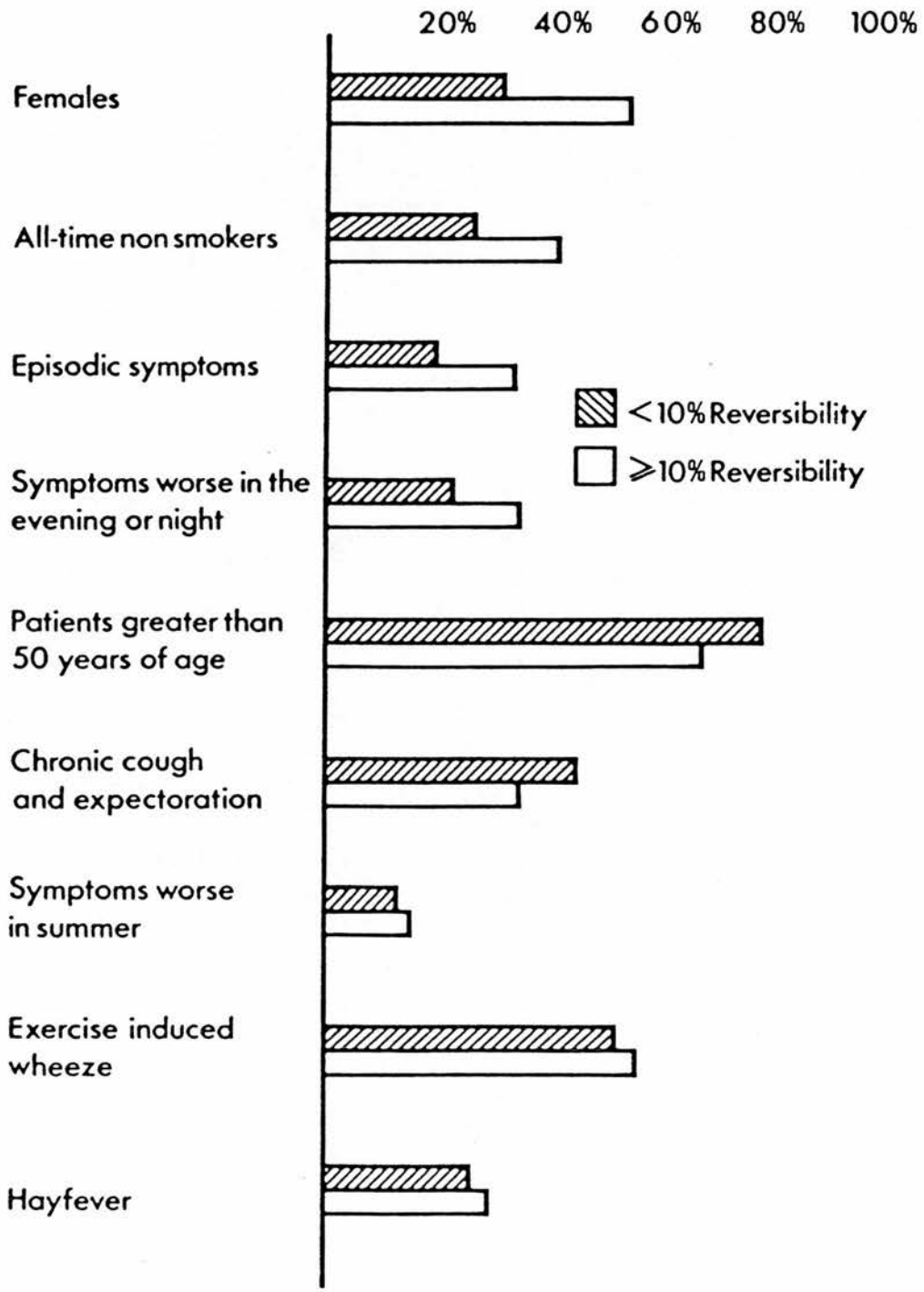


Figure 10

The value of the discriminant function in predicting bronchodilator reversibility by patient characteristics and symptoms

	Predicted poor (<10%) reversibility	Predicted good (≥10%) reversibility	Total number of patients
Poor (<10%) reversibility	75(64%)	43(36%)	118
Good (≥10%) reversibilty	36(37%)	61(63%)	97

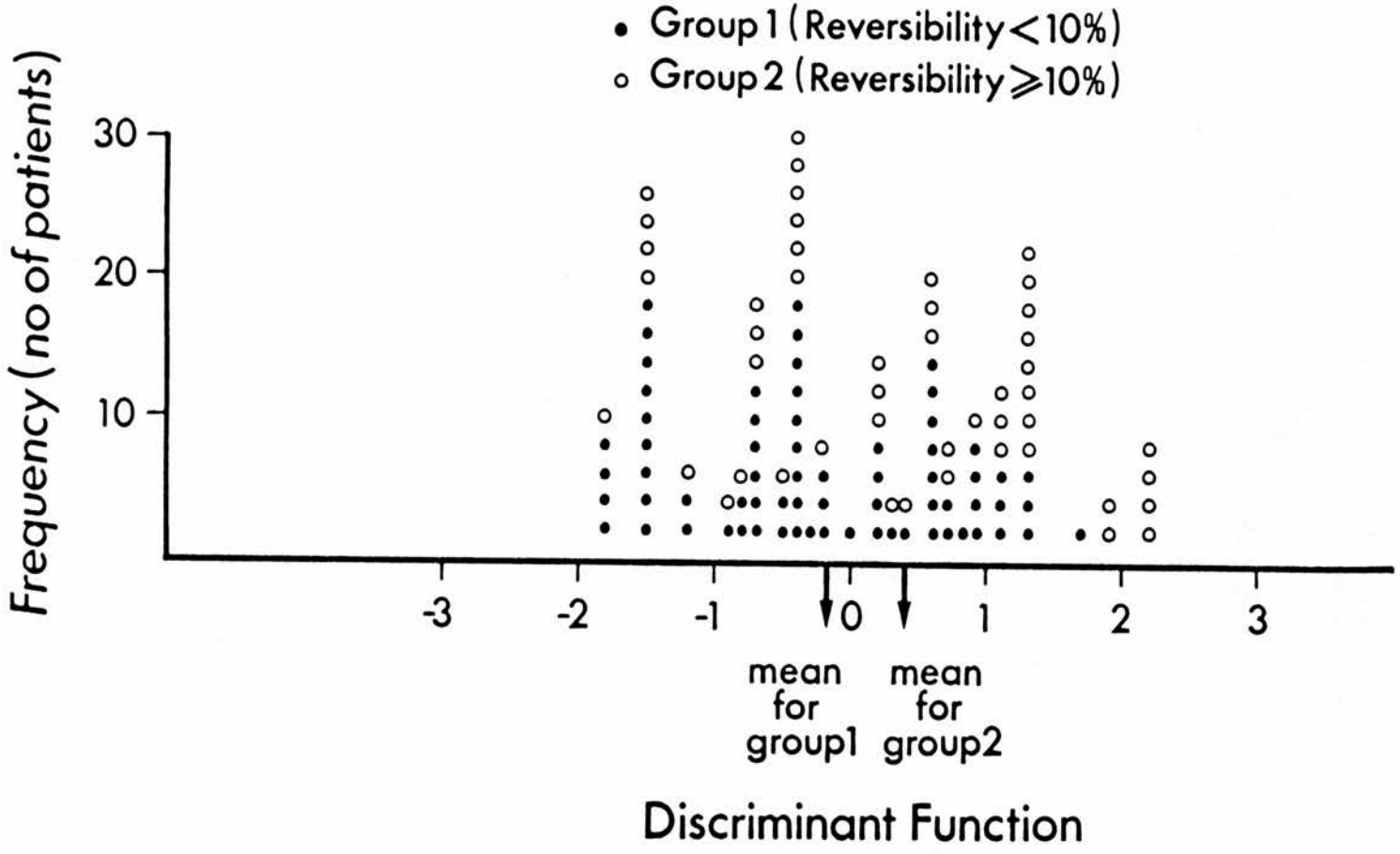
Relative risk 1.71

Table 28.

Bronchodilator reversibility by the general practitioner and predicted diagnosis using the discriminant function.

	Bronchodilator reversibility (change in PEFR expressed as a % of the predicted PEFR)		
	<10%	≥10%	Total number of patients
Group A	60(50%)	60(50%)	120
Group B	58(61%)	37(39%)	95
Predicted group A	52(48%)	57(52%)	109
Predicted group B	66(62%)	40(38%)	106

Table 29



STACKED HISTOGRAM OF THE DISCRIMINANT FUNCTION OF PATIENTS WITH BRONCHODILATOR REVERSIBILITY EQUAL TO OR ABOVE 10% OR BELOW 10%

FIGURE 11

b) CORTICOSTEROID REVERSIBILITY STUDIES.

145 patients (67 asthmatics and 78 chronic bronchitics) had a PEFR less than 60% of the predicted value. 18(12%) of these already took oral corticosteroid therapy. 17(12%) had taken oral corticosteroids in the past and did not wish to take a further course.

37(34%) of the remaining 110 patients were given a trial of oral corticosteroids. Other patients were excluded for the following reasons:-

1) 25(23%) Congestive cardiac failure, hypertension, ischaemic heart disease.

2) 13(12%) Peptic ulceration or severe indigestion.

3) 6(5%) Known old tuberculosis.

4) 3(3%) Mental illness.

5) 3(3%) Diabetes Mellitus.

6) 4(4%) Miscellaneous medical disorders (intercurrent chest infection, epilepsy, malignancy)

7) 4(4%) A history of a previous adverse reaction to oral corticosteroids.

8) 4(4%) An inability to comply with taking PEFR recordings.

9) 11(10%) An unwillingness to take oral corticosteroids.

Of 37 patients given a trial of oral corticosteroids 1 failed to attend for follow up (despite 3 appointments made for him), and another 2 patients returned having failed to take all the tablets (They did not complain of having had side effects but were worried about taking corticosteroid therapy,). The remaining 34 patients took the full course of placebo and prednisolone tablets. This treatment was well tolerated though 2 patients complained of feeling bloated

and one of hot flushes throughout the prednisolone therapy. No serious side effects were encountered.

26 of the 34 (76%) patients completed a peak flow graph on their chart entirely correctly including all 28 recordings (twice daily for two weeks). A further 2 patients provided all recordings but did not complete the graph correctly. 3 patients omitted one recording, and a further 2 omitted up to half the recordings. In only one patient could no valid assessment be made from the peak flow chart.

Tables 30 and 31 illustrate the symptomatic characteristics and reversibility of the 33 patients who undertook a full trial of oral corticosteroids. In this group there were 15 females and 18 males, their mean age was 57.3 years (range 23-73 years). 15 were in group A, and 18 in group B. In 4 cases diagnosed by their general practitioners as asthmatic, the discriminant function had given a "predicted diagnosis" of chronic bronchitis. 13 of the 18 patients in group B and 4 of the 15 in group A fulfilled the M.R.C. criteria for chronic bronchitis with chronic cough and expectoration.

Corticosteroid reversibility was assessed by two methods:
1) By comparing the mean PEFRs of the last 5 days (10 recordings) during placebo and prednisolone therapy (the change in mean PEFR being expressed as a percentage of the mean initial PEFR during placebo therapy).
2) By undertaking paired t tests on the untransformed data on both morning and evening recordings separately.
The most significant of the two t tests for each patient is included in table 31. In 3 patients t tests revealed a significant response ($p<0.05$) for evening recordings only, in all other responders, this

The characteristics of 33 patients undertaking a trial of oral corticosteroid therapy.

Patient number	Age (yrs)	Sex	Chronic cough and expect'n	Smoking history	Hay-fever	Exercise induced wheeze
1	35	F	no	no	yes	yes
2	56	F	yes	yes	no	no
3	23	F	no	no	no	yes
4	65	F	no	ex	no	no
5	72	F	yes	no	yes	yes
6	25	M	yes	ex	yes	yes
7	67	M	no	yes	no	no
8	64	F	yes	ex	no	yes
9	52	M	yes	ex	no	yes
10	67	M	yes	yes	no	no
11	70	M	yes	ex	no	no
12	73	M	no	yes	no	yes
13	55	F	yes	yes	no	no
14	60	M	yes	yes	no	no
15	62	F	no	yes	yes	no
16	67	M	yes	ex	no	no
17	46	F	no	yes	no	yes
18	72	M	yes	yes	no	no
19	49	F	no	ex	no	yes
20	66	F	yes	ex	no	no
21	55	F	no	yes	no	no
22	51	M	no	ex	no	no
23	28	F	no	no	no	yes
24	73	M	no	ex	no	no
25	60	M	yes	yes	no	no
26	66	M	no	no	no	yes
27	60	F	no	no	no	yes
28	62	M	no	no	no	yes
29	66	M	yes	ex	no	no
30	60	F	no	ex	no	no
31	63	M	yes	ex	no	yes
32	28	M	yes	no	yes	yes
33	71	M	yes	yes	no	yes

yes=present smoker
no=all-time non-smoker
ex=previous smoker

Table 30

The reversibility of 33 patients given a trial of oral corticosteroid therapy.

Patient number	Group	Predicted group	% Reversibility	t-value and significance
1	A	A	5%	1.0 NS
2	B	B	36%	6.7 P<0.01
3	A	A	101%	5.3 p<0.01
4	B	B	-2%	0.4 NS
5	A	A	25%	3.0 p<0.05
6	A	A	61%	10.5 p<0.001
7	B	B	24%	5.4 p<0.01
8	B	B	59%	7.0 p<0.01
9	B	B	7%	0.2 NS
10	B	B	18%	3.0 p<0.05
11	B	B	0%	0.3 NS
12	B	B	-4%	0.2 NS
13	B	B	2%	2.4 NS
14	B	B	-2%	1.0 NS
15	A	A	5%	0.9 NS
16	A	B	7%	1.8 NS
17	A	A	0%	0.1 NS
18	B	B	4%	6.0 P<0.01
19	A	B	21%	9.0 P<0.01
20	B	B	3%	2.2 NS
21	B	B	6%	1.9 NS
22	A	B	25%	5.0 P<0.01
23	A	A	15%	1.7 NS
24	A	B	10%	1.9 NS
25	B	B	0%	1.0 NS
26	A	A	22%	6.3 P<0.01
27	A	A	25%	5.7 P<0.01
28	A	A	15%	5.9 P<0.01
29	B	B	7%	1.6 NS
30	B	B	7%	2.7 NS
31	B	B	-1%	0.4 NS
32	A	A	-28%	2.4 NS
33	B	B	-2%	0.4 NS

Table 31

occurred in both morning and evening recordings. The use of t test significance ($p<0.05$) and a change in mean PEFR of 15% or greater as response criteria gave entirely similar results apart from 2 patients (numbers 18 and 23).

The symptoms indicated in table 30 were analysed in both responders and non-responders (change in PEFR $\geq$15% and <15% respectively), there was no significant difference in the incidence of any of these symptoms between the two groups.

The use of the discriminant function "predicted diagnosis" did not change the number of responders between the diagnostic groups. Approximately 6 in 10 asthmatics and 1 in 4 of the chronic bronchitics had "good" corticosteroid reversibility (see table 32). The relationship between corticosteroid and bronchodilator reversibility is illustrated in figure 12. The correlation between these two responses was significant ($r= 0.403$, $p<0.05$ Spearman's test).

In order to assess whether there was a placebo response during the corticosteroid trials, the means of the first and last 4 recordings during the placebo week were compared (morning and evening recordings on days 1-2 and 6-7 respectively). The mean difference between these periods in the whole group was 13.6. Though this difference was not significant ($t=1.92$ DF32 N.S.) the graphs of two patients (illustrated in figure 13) revealed marked individual placebo responses.

The importance of diurnal variation was assessed by expressing the difference in mean morning and evening recordings for each patient as a percentage of the mean peak flow during the whole placebo week. Paired t tests were undertaken on the untransformed

The number of corticosteroid responders (an improvement of 15% or greater) by the general practitioner and discriminant function "predicted" diagnoses.

	<15%	≥15%	Total number of patients
Group A	6(40%)	9(60%)	15
Group B	14(78%)	4(22%)	18
			33
Predicted group A	4(37%)	7(63%)	11
Predicted group B	16(73%)	6(27%)	22
			33

Table 32.

THE RELATIONSHIP BETWEEN BRONCHODILATOR AND CORTICOSTEROID REVERSIBILITY

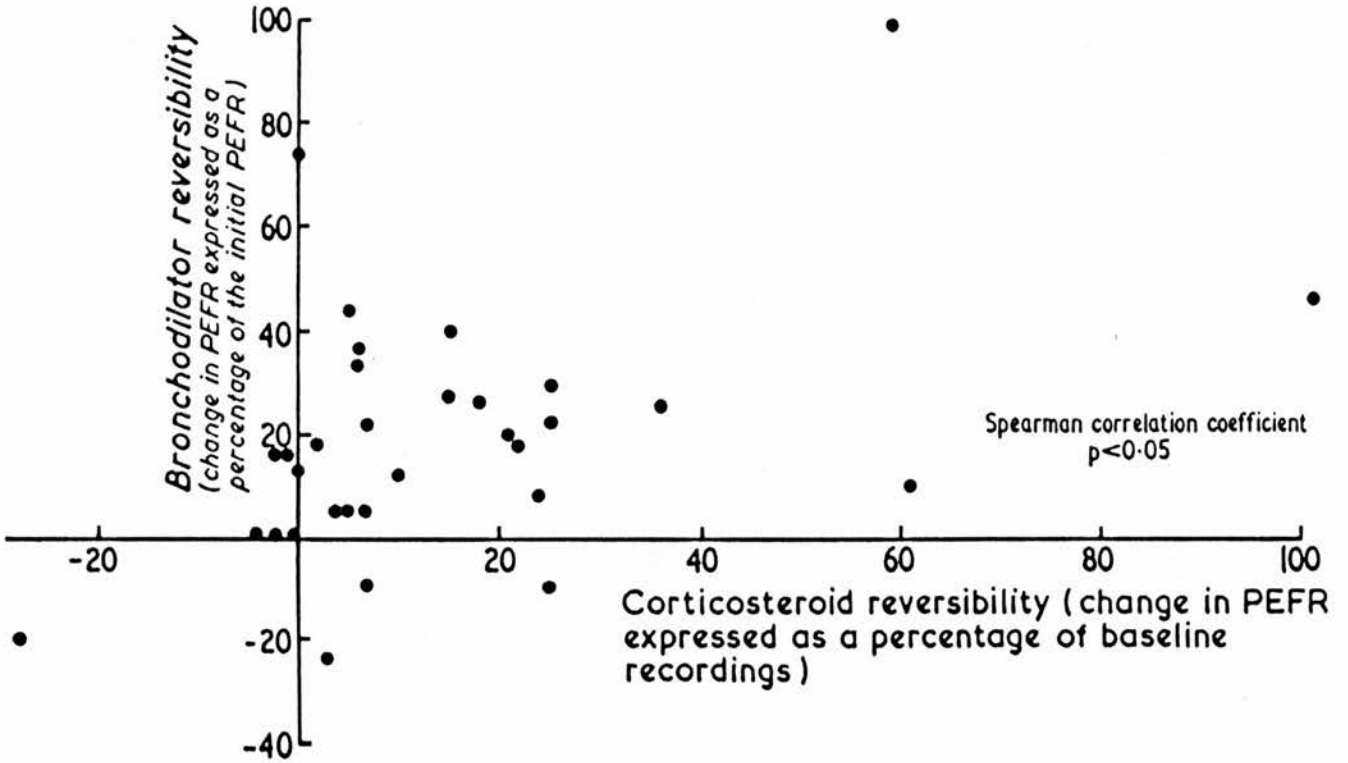


FIGURE 12

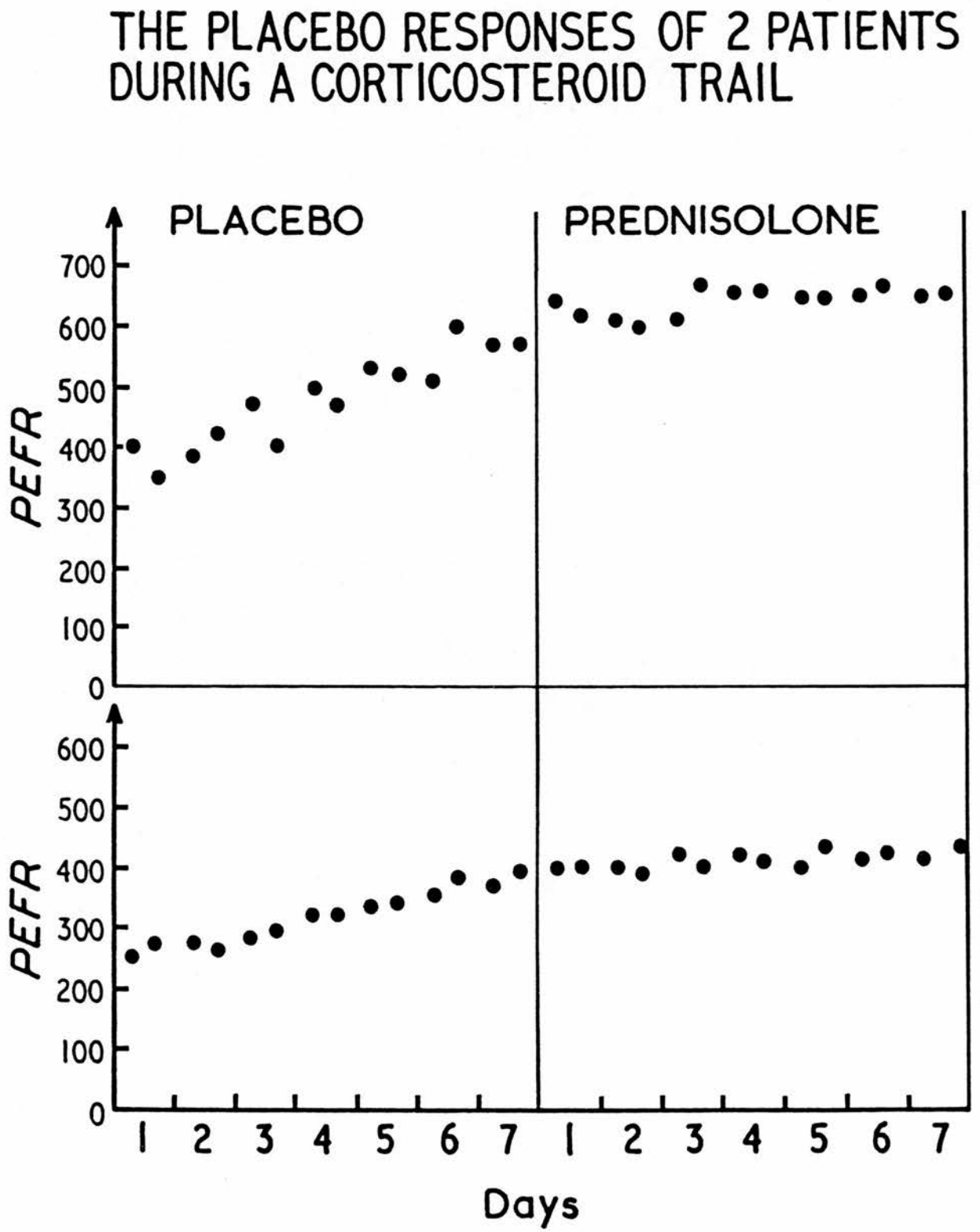

THE PLACEBO RESPONSES OF 2 PATIENTS DURING A CORTICOSTEROID TRAIL
PLACEBO
PREDNISOLONE
PEFR
700
600
500
400
300
200
100
0
Pat No 6
PEFR
600
500
400
300
200
100
0
Pat No 7
1 2 3 4 5 6 7 1 2 3 4 5 6 7
Days

FIGURE 13

data in order to ascertain whether morning and evening recordings were significantly different in each patient. The results are analysed in table 33. The mean evening recordings were significantly higher than those in the morning ($t=2.58$ DF29 $p<0.05$). The mean difference in PEFR was slightly less in group A (4.9%) than in group B (5.5%). When examining individual patients, 3 asthmatics and 3 chronic bronchitics were found to have significantly higher ($p<0.05$) evening than morning recordings. In 4 of these (1 asthmatic and 3 chronic bronchitic), this difference in peak flow rate was greater than 20%. There was no correlation between diurnal variation measured in this way and corticosteroid reversibility ($r= -0.028$).

c) THE TREATMENT OF PATIENTS WITH DOCUMENTED REVERSIBILITY.

The therapy of those patients responding (by 15% or more) to the corticosteroids trial was examined. Of the 13 responsive patients, 3 took inhaled corticosteroids (2 in group A and 1 in group B) and 2 sodium cromoglycate (both in group A). 4 out of the 5 patients using inhaled prophylaxis were prescribed below standard doses (<400mcg beclomethasone diproprionate or <4 capsules of sodium cromoglycate daily or equivalents) despite scores of 2 or 3 for day or night time symptoms.

12 out of the 13 responsive patients had scores of 2 or 3 for day or night time symptoms, suggesting that in nearly all this group prophylactic therapy with at least standard doses of inhaled corticosteroid was warranted.

45 patients (32 in group A and 13 in group B) were shown to have good bronchodilator reversibility (15% or greater of the predicted PEFR) but did not have a trial of oral corticosteroids. 24(53%) of these patients (15 in group A, 9 in group B) had scores of

The diurnal variation during the placebo week of the corticosteroid trials.

Pat No	Group	Mean AM PEFR	Mean PM PEFR	Difference of mean AM & PM PEFR as % of mean PEFR	t-test & significance
1	A	171	168	-2%	0.6 NS
2	B	125	128	2%	0.7 NS
3	A	118	140	17%	1.0 NS
4	B	121	131	8%	0.7 NS
5	A	480	475	-1%	0.2 NS
7	B	310	321	3%	2.2 NS
8	B	74	85	11%	1.1 NS
9	B	198	212	7%	0.8 NS
10	B	154	205	27%	4.0 p<0.01
11	B	160	158	-1%	0.1 NS
12	B	147	146	-1%	0.1 NS
13	B	128	166	26%	7.6 p<0.001
14	B	205	250	20%	8.3 p<0.001
16	A	185	201	8%	4.2 p<0.01
17	A	193	224	15%	4.0 p<0.01
18	B	204	206	1%	0.5 NS
20	B	134	136	1%	0.2 NS
21	B	120	136	12%	1.2 NS
22	A	188	178	-5%	2.3 NS
23	A	177	244	32%	3.1 p<0.05
24	A	302	319	5%	0.7 NS
25	B	240	250	4%	1.6 NS
26	A	171	166	-3%	0.7 NS
27	A	105	91	-14%	1.3 NS
28	A	138	143	3%	1.3 NS
29	B	115	117	2%	0.1 NS
30	B	98	80	-20%	2.0 NS
31	B	240	234	-3%	0.7 NS
32	A	273	283	4%	0.5 NS
33	B	247	250	1%	0.2 NS

3 patients omitted because of insufficient data

Table 33.

2 or 3 for day or night time symptoms. The treatment of this symptomatic group is illustrated in table 34. All 6 symptomatic patients on inhaled corticosteroids and 3 out of the 5 on sodium cromoglycate took below standard dosage of these drugs.

c) DISCUSSION

When bronchodilator reversibility was expressed as the change in PEFR as a percentage of the initial value, there was no significant difference between the asthmatics and chronic bronchitics. However, the chronic bronchitics had lower initial PEFRs than the asthmatics, and when reversibility is expressed in this manner responses at low initial values may be exaggerated (Nicklaus et al 1969). In an attempt to increase the specificity of the reversibility studies the change in PEFR was expressed as a percentage of the predicted PEFR. Bronchodilator reversibility expressed in this manner was significantly higher in the asthmatics but again there was a great overlap with the chronic bronchitics. Using this method a reversibility of 15% has been found to be specific for asthma (Nicklaus et al 1969). In this study only a reversibility greater than 20% was specific for asthma (general practitioner and predicted diagnoses).

The degree of reversibility found in the chronic bronchitics in this study may be considered to be surprising; however, Curtis et al (1966) found that 84 out of 100 patients with chronic bronchitis and emphysema showed improvement with isoprenaline, and although the FEV1 declined in this group over a 5 year period this reversible element remained. Crompton (1968) examined the effects of bronchodilators and corticosteroids on 18 asthmatics and 18 chronic bronchitics and found that the mean reversibility to isoprenaline was

The treatment of symptomatic patients with bronchodilator reversibilty equal to or greater than 15% (the change in PEFR being expressed as a percentage of the predicted norm) in whom a corticosteroid trial was not undertaken.

	Diagnostic group	
	A	B
Number of patients	15	9
Number of patients using:-		
Bronchodilators alone	3	6
Bronchodilators + sodium cromoglycate	5	0
Bronchodilators + inhaled corticosteroid	3	3
Bronchodilators + oral corticosteroid	4	0

Table 34.

32% (of the initial value). It has been considered that a reversibility greater than 25% is suspicious of asthma (Crompton 1980) and yet 11 out of the 18 chronic bronchitics in Crompton's study demonstrated this degree of reversibility to isoprenaline.

A comparison of symptoms in patients with good and poor bronchodilator reversibility emphasises the poor correlation between the two, and that reversibility cannot be predicted from the symptomatic history. Why was there such a poor relationship between the practitioners' diagnoses or the symptomatic "predicted" diagnoses and the bronchodilator reversibility? Hume and Rhys-Jones (1960) have stated that the response of an asthmatic to a bronchodilator depends upon the degree of initial airways obstruction present. If this were true then each patient would have a range of bronchodilator reversibility depending on the degree of initial airways obstruction. In this study patients with severe airways obstruction had similar responses to those with mild obstruction. This may have been due to the fact that all the patients seen were in a stable state, despite the fact that some had severe airways obstruction. The observation by Hume and Rhys-Jones was undertaken on a very small number of asthmatics and more work is required to examine the reproducibility of the bronchodilator reversibility in airways obstruction. If a single study is an unreliable measure of response, perhaps the specificity of bronchodilator reversibility to asthma could be enhanced by undertaking repeated studies over a period of time and documenting the mean of several results.

Very few patients reached their predicted PEFR with standard doses of salbutamol, and it is possible that the specificity of these tests could be increased by the use of higher doses of

bronchodilator. Certainly some asthmatics require higher than standard doses of a $\beta 2$ stimulant to demonstrate maximal reversibility (Prior and Cochrane 1982). Unfortunately it is not known whether patients with chronic bronchitis respond to a similar degree with higher doses of $\beta 2$ stimulants as those with asthma.

The idea of a trial of oral corticosteroid therapy in chronic asthma to assess which patients would benefit from long-term therapy was described nearly 30 years ago (Walsh and Grant 1966) and it is now standard practice. Although the effect of corticosteroids in chronic bronchitis is more controversial (Sahn 1978), it is now recommended that a trial of such therapy should be given to any such patients with disabling symptoms (Royal College of Physicians 1981, Editorial 1980).

Corticosteroid trials were used in this study, firstly, to investigate whether there was a relationship between the general practitioners' diagnoses or the "predicted" symptomatic diagnoses and the reversibility to corticosteroids, and secondly, to demonstrate how many patients with disabling airways obstruction, despite treatment from their general practitioner, could benefit from this form of therapy. None of the patients studied had an acute exacerbation of symptoms; this is important as there is now evidence that corticosteroids are valuable in acute exacerbations of chronic bronchitis (Albert et al 1980).

Because the corticosteroid trials were undertaken independently of the general practitioners' management, strict criteria were used to exclude patients with associated medical conditions which might be worsened by such treatment. High dose corticosteroids may cause fluid retention, increase the blood

pressure, disturb glucose homeostasis, induce acute psychosis and cause peptic ulceration (this latter effect remains unproven) (Cochrane 1983). Despite such side effects, the results of this study confirm the safety of short courses of oral corticosteroids. Used in this manner there is little suppression of adrenal function (Webb and Clark 1981b) and the course may be terminated abruptly without risk. It was surprising how many patients in this study were excluded from having a corticosteroid trial because of associated medical conditions. Such conditions are only relative contraindications, however, and in normal clinical practice more trials could have been undertaken if considered medically justified.

The majority of patients completed their peak flow charts correctly. Hetzel suggested that patients found it easier merely to record the peak flow values numerically on a chart rather than produce a graph (Hetzel et al 1979). In this study only 9% were unable to formulate a graph and the omission of recordings was a more frequent error.

Although no statistically significant placebo response was demonstrated in the group as a whole, some patients demonstrated a marked response to placebo highlighting some of the pitfalls in the interpretation of therapeutic trials in obstructive airways disease. Most previous workers (Webb et al 1981a, Stokes et al 1982, Lam et al 1983) have also failed to demonstrate a placebo response, whilst others think it important (Mitchell et al 1984). At present few chest physicians routinely use placebo tablets, and one could not expect this of the general practitioner.

There are few guidelines for the assessment of corticosteroid trials. In keeping with previous experience (Webb et al 1981a)

undertaking paired t tests on the data offered little advantage over the much simpler analysis of calculating the mean percentage improvement. Many workers determine the corticosteroid response by visual assessment of the PEFR chart. In order to clarify the trends in the PEFR, the use of cusum (cumulative sum) analysis has been suggested (Clarkson et al 1978), and was considered in this study, using the mean of the first two days recordings on placebo therapy as the reference value. The use of this analysis in a small selected sample did not appear to improve on mere visual inspection of trends in PEFR on the charts. Because it is highly subjective, visual assessment of the peak flow charts was not documented.

Some patients improved symptomatically on oral corticosteroid therapy but not by recordings of the peak flow chart. Such patients are difficult to assess. They may have been experiencing the non-specific euphoria, which occurs with corticosteroid therapy. However, some patients fail to respond by PEFR or FEV1, but show improvement in the FVC or measurements of exercise capacity such as the 12 minute walk (Williams and McGavin 1980). In others, there is a reduction in total lung capacity because of a decrease in the hyperinflation of the lungs which occurs in obstructive airways disease (Turner-Warwick 1977). It is impossible, without further assessment, to know how many patients in the study with a symptomatic response to corticosteroids had derived a physiological benefit from the drug.

Two young patients in the study (numbers 1 and 32) with typical asthma (atopy and episodic wheezing) had little response to corticosteroids as measured by the PEFR. Perhaps higher doses or longer courses of corticosteroids were required. In assessing the

time course of response to corticosteroids (using the same dose of prednisolone as in this study) Webb et al (1981a) found that 10 out of 13 responsive patients had reached their maximum response within 7 days. It is accepted therefore, that some responders may have been missed. Prednisolone treatment for one week was chosen as a compromise between that most likely to identify responders and that least likely to incur side effects.

The proportion of responders was similar by both the general practitioner and the "predicted" symptomatic diagnoses. The latter did not help, therefore, in predicting reversibility. Although corticosteroid responsiveness was more likely to occur in those with an asthmatic symptomatology with 7 out of 11 responders, there were 6 out of 22 responders in those with symptoms of chronic bronchitis. Previous workers have found that a history of wheezing attacks and a short duration of symptoms (Petty et al 1970), a variability of symptoms (Lam et al 1983) and sputum eosinophilia (Shim et al 1978) have all been associated with a good response to corticosteroid therapy. However, this study suggests that there is a range of corticosteroid responsiveness in obstructive airways disease which is poorly correlated with symptoms.

As with the bronchodilator studies this may be due to inadequacies in the tests and the expression of the results. However, the reason for the poor correlation between the symptomatic diagnosis and the bronchodilator and corticosteroid reversibility may be more fundamental than this. In the introduction it was noted, in a discussion of the Dutch hypothesis, that bronchial reactivity in patients with typical chronic bronchitis ranged from normal to the hyper-reactivity usually associated with asthma. This heterogeneity

of response to histamine or methacholine in chronic bronchitis also applies to the response to drug therapy. Thus there is a range of reversibility from that usually associated with asthma to the minimal response of fixed airways obstruction. One would expect, therefore, an overlap in reversibility between patients with asthma and chronic bronchitis. This may be due to the fact that the underlying mechanism of airways obstruction is similar despite the differing causative factors such as allergy and smoking. Although unproven, those patients with little airways reversibility may have predominant emphysema. As mentioned earlier this is a difficult diagnosis to make accurately in life. Although corticosteroid reversibility has been considered previously to be a universal feature of asthma, it is now recognised that there are some patients with a typical history of the disorder who are resistant to the drug (Carmichael et al 1981). In this study, as previously described, there were two young patients with typical asthma who did not respond to corticosteroids.

Asthmatics (Hetzel and Clark 1980) unlike chronic bronchitics (Dawkins and Muers 1981) have large diurnal variations in airways obstruction, so much so that an amplitude greater than 20% from the mean has been considered to be a useful screening test for asthma (Hetzel and Clark 1980). However, such studies have used cosinar analysis to identify the diurnal rhythm, which is impracticable in clinical practice. As asthma is often associated with an increase in airways obstruction in the early morning (Turner-Warwick 1977) it was thought worthwhile to examine whether twice daily recordings of PEFR could help in the differentiation between asthma and chronic bronchitis. In this study the mean evening peak flow rates were significantly higher than the morning values by

5.3% (of the mean peak flow rate). This was similar to previous experience (Webb et al 1981), though it was surprising that the variation was slightly higher in the chronic bronchitics than the asthmatics. There was no relationship between corticosteroid reversibility and diurnal variation, and this type of simple analysis would appear to be of dubious value.

In practice the main aim of undertaking a corticosteroid trial is to identify those patients who would benefit from long term treatment with this drug. Once responsiveness has been demonstrated, many of these patients can be maintained on inhaled therapy alone (Toogood et al 1978). However, it is likely that there are degrees of responsiveness and in some patients the documented improvement obtained during a corticosteroid trial may be impossible to maintain even with long term oral corticosteroids (Stokes et al 1982).

In this study the corticosteroid trials identified a group of symptomatic yet responsive patients, none of whom had been taking satisfactory maintenance therapy. It is likely that the majority would have benefitted from inhaled corticosteroid in adequate dosage. Though bronchodilator reversibility need not imply corticosteroid responsiveness (Carmichael et al 1981), the findings of this study and other workers suggest that there is a relationship. It is possible, therefore, that those patients with good bronchodilator reversibility in whom a corticosteroid trial was not undertaken may also have improved on inhaled corticosteroids.

The number of patients exhibiting various characteristics and symptoms with bronchodilator reversibility (the change in PEFR expressed as a percentage of the predicted norm) equal to and above 10%,or below 10%

	<10%	≥10%
Number of patients	118	97
Number of females	38(32%)	53(55%)
	X^2 10.9 DF1 p<0.001	
Number of all time non-smokers	32(27%)	41(42%)
	X^2 5.4 DF1 p<0.05	
Number with episodic symptoms	24(20%)	33(34%)
	X^2 5.1 DF1 p<0.05	
Number with symptoms worse in the evening or night	27(23%)	34(35%)
	X^2 3.8 DF1 p<0.05	
Number >50yrs of age	93(79%)	66(68%)
	X^2 3.2 DF1 NS	
Number with chronic cough and expectoration	53(45%)	34(35%)
	X^2 2.1 DF1 NS	
Number with symptoms worse in summer	15(13%)	15(15%)
	X^2 0.3 DF1 NS	
Number with exercise induced wheeze	60(51%)	53(55%)
	X^2 0.3 DF1 NS	
Number with hayfever	31(26%)	28(29%)
	X^2 0.2 DF1 NS	
Number with wheeze in contact with animals	20(17%)	17(18%)
	X^2 0.0 DF1 NS	

Table 27.

CHAPTER APPENDIX

CHAPTER 6

GENERAL ASPECTS OF MANAGEMENT AND BRONCHODILATOR THERAPY

a) General aspects of management

b) The prescription of bronchodilators

c) Inhaled bronchodilators

d) Oral bronchodilators

e) Side effects

f) Patient preference

g) Other forms of therapy for obstructive airways disease

h) Discussion

a) GENERAL ASPECTS OF MANAGEMENT

Hospital or chest clinic outpatient attendance-

141(70%) patients in group A and 64(57%) in group B had attended a hospital outpatient department or chest clinic with symptoms of airways obstruction at sometime; 51(25%) in group A and 23(20%) in group B had attended within the previous 12 months.

General practice surgery attendance-

The number of times patients in groups A and B had attended their general practitioner in the previous six months is indicated in table 35 (visits for repeat prescriptions without seeing the doctor and emergency housecalls are excluded). Patients in groups A and B had similar attendance rates with approximately two thirds attending at least twice in the previous six months. The differences in hospital clinic attendance, frequency of visits to the general practitioner, and the proportion who were satisfied with the control of their symptoms between the four practice centres are illustrated in table 36. Approximately a quarter of patients were currently attending hospital outpatient clinics, this proportion was similar in all practice centres. There were insignificant differences in the rates of attendance with the general practitioner and the proportion satisfied with the control of their symptoms between the practice centres. However, it is noticeable that the practice with the lowest attendance rates had the smallest number of patients who were satisfied with their symptom control.

A similar proportion of hospital outpatient attenders in groups A and B frequently (greater than 5 attendances in 6 months) visited their general practitioner (11 out of 74, 15%) as those who did not attend hospital outpatients (39 out of 240, 16%).

Attendance at the general practice surgery.

The number of patients attending their general practice surgery in the previous 6 months

	Group A	Group B
Never	21(10%)	2(2%)
Once	59(29%)	26(23%)
2-5 times	88(44%)	68(60%)
>5 times	33(16%)	17(15%)
Number of patients	201	113

Table 35.

Hospital clinic and general practice surgery attendance between the general practice centres.

Practice centre	1	2	3	4
Number of patients	140	45	62	67
Number having attended hospital outpatients in the previous 12 months	34(26%)	12(26%)	16(26%)	11(17%)

Number of patients attending their general practice surgery in the previous 6 months.

Never	10(7%)	5(11%)	2(3%)	6(9%)
Once	31(22%)	21(47%)	10(16%)	23(34%)
2-5 times	76(54%)	17(38%)	35(56%)	28(42%)
>5 times	23(16%)	2(4%)	15(24%)	10(15%)

The number of patients satisfied with the control of their symptoms.

116(83%)	30(67%)	46(74%)	48(72%)

Table 36.

b) THE PRESCRIPTION OF BRONCHODILATORS.

284 out of 314 (90%) patients in groups A and B and all patients in group H used a bronchodilator. 28 of the remaining patients in groups A and B used a prophylactic drug alone (including 19 using sodium cromoglycate, 7 inhaled corticosteroids, and 2 systemic corticosteroids). 18 of these 28 patients (64%) used their prophylactic drug on demand for wheezing attacks, suggesting the need for bronchodilator therapy. A further 2 patients had recently stopped all therapy.

The different types of bronchodilator delivery prescribed to the 284 patients in groups A and B are summarised in table 37. Significantly more chronic bronchitics used oral therapy than asthmatics, this difference continued to apply in a separate analysis of patients over 50 years of age, and there was little difference in bronchodilator delivery between asthmatics over and under 50 years of age. There was also a significant difference in the use of inhaled and oral drugs between those asthmatics attending hospital clinics (groups A-OPD, and H) and those attending their general practitioner alone (group A-GP) with more of the latter using oral bronchodilators (see table 38). When the type of bronchodilator delivery was examined in the asthmatics between the four practice centres, again differences were found with between 2-36% using oral therapy alone (see table 39).

c) INHALED BRONCHODILATORS.

The types of inhaled bronchodilators prescribed to patients in groups A, B, and H are illustrated in table 40. The great majority used β stimulant inhalers with ipratropium bromide being used mainly by chronic bronchitics. There was little difference in the type of

The number (%) of asthmatics (group A) and chronic bronchitics (group B) using inhaled and/or oral bronchodilators.

	Groups			
	A	B	A	B
	All patients		Patients >50yrs	
Number(%) using bronchodilators	172	112	83	105
Number(%) using bronchodilator inhalers alone	104(60%)	31(28%)	43(52%)	28(27%)
Number(%) using oral bronchodilators alone	30(17%)	51(46%)	13(16%)	48(46%)
Number(%) using combined oral and inhaled bronchodilators	38(22%)	30(27%)	27(33%)	29(28%)
	X^2 34.3 DF2 p<0.001		X^2 23.7 DF2 p<0.001	

Table 37.

The number (%) of patients using various types of bronchodilator delivery in groups A-GP, A-OPD and H.

	Group		
	A-GP	A-OPD	H
Number(%) using a bronchodilator	126	46	48
Number(%) using an inhaled bronchodilator alone	75(60%)	29(63%)	34(71%)
Number(%) using oral bronchodilator alone	27(21%)	3(7%)	1(2%)
Number(%) using combined oral and inhaled bronchodilator therapy	24(19%)	14(30%)	13(27%)
	$X^2$14.6 DF4 p<0.01		

Table 38.

The number(%) of asthmatics (group A) using the various types of bronchodilator delivery between the practice centres.

	Practice centre			
	1	2	3	4
Number of patients using a bronchodilator	72	25	26	49
Number(%) using inhaled therapy with or without an oral bronchodilator	53(74%)	21(84%)	20(77%)	48(98%)
Number(%) using oral bronchodilator therapy alone	19(36%)	4(16%)	6(23%)	1(2%)
		X^2 12.3 DF3 p<0.01		

Table 39.

The types of inhaled bronchodilators prescribed in groups H, A and B.

	Groups		
	H	A	B
Number of patients using inhalers	47	142	61
Number(%) using aerosol inhalers	44(94%)	134(94%)	58(95%)
Number(%) using dry powder inhalers	3(7%)	8(6%)	3(5%)
Number(%) using the following drugs:			
β2 stimulants	47(100%)	139(98%)	54(87%)
Non selective adrenergic stimulants	0	2(1%)	2(3%)
Ipratropium bromide	0	2(1%)	9(14%)

Table 40.

inhaler used between groups A and H.

Regular or demand use of inhalers-

Asthmatics attending hospital outpatient clinics (groups A-OPD, and H) were more likely to take regular therapy than those attending their general practitioner alone (group A-GP). This difference continued to apply when analysing only patients with moderate or severe day time symptoms in whom two thirds of groups A-OPD and H took regular therapy in contrast to only a seventh of group A-GP (see table 41). Similar findings were obtained in the chronic bronchitics, with more of those patients attending hospital clinics within the previous 12 months (group B-OPD) taking regular inhaled therapy than those who attended their general practitioner alone (group B-GP) (see table 42).

Dosage of bronchodilator inhalers-

The dosages of bronchodilator inhalers used are included in table 43. The majority of patients (81%) used salbutamol. In group A 10 out of 29 patients (34%) taking more than 8 puffs daily of their bronchodilator inhaler did not use inhaled corticosteroid or sodium cromoglycate. 26 of these 29 patients had scores of 2 or 3 for day or night time symptoms. All patients in group H using these doses also took such prophylactic therapy. Only 7 patients (3%) in groups A and B used more than 16 puffs daily.

In groups A and B 17 patients (8% of inhaler users) were regarded as underusing their inhalers (taking less than 2 puffs daily despite scores of 2 or 3 for day or night time symptoms). Significantly more patients ($p<0.001$) underusing aerosol inhalers had a poor inhaler technique (11 out of 17,65%) compared with those taking above standard dosage (greater than 8 puffs daily) (4 out of

The regular use of bronchodilator inhalers in groups H, A-OPD, and A-GP

	Groups		
	H	A-OPD	A-GP
Number of patients using broncho-dilator inhalers	47	43	99
Number(%) taking regular doses (without regard to symptoms)	23(48%)	13(30%)	12(12%)
	X^2 23.5 DF2 p<0.001		
Number of inhaler users with scores of 2 or 3 for day time symptoms.	22	19	44
Number(%) taking regular doses (without regard to symptoms)	15(68%)	11(58%)	6(14%)
	X^2 23.6 DF2 P<0.001		

Table 41.

The regular use of bronchodilator inhalers in groups B-OPD and B-GP.

	Groups	
	B-OPD	B-GP
Number(%) of patients using bronchodilator inhalers	18	43
Number(%) taking taking regular doses	13(72%)	17(40%)
	X^2 5.4 DF1 p<0.05	
Number of bronchodilator inhaler users with a score of 2 or 3 for daytime symptoms	14	28
Number(%) taking regular doses	13(93%)	11(39%)
	X^2 10.9 DF1 p<0.001	

Table 42.

The dosages of inhaled bronchodilators used in groups H, A, and B.

	Groups		
	H	A	B
Number of patients using bronchodilator inhalers	47	142	61
Daily dosage:			
>16 puffs	0(0%)	6(4%)	1(2%)
9-16 puffs	11(23%)	23(16%)	8(13%)
<9 puffs	36(77%)	113(80%)	52(85%)
<2 puffs despite a score of 2 or 3 for daytime symptoms	0(0%)	7(5%)	10(16%)

For simplicity, in this table 1Rotacap = 2puffs. Unless the patient was using ipratropium bromide alone,these dosages relate to the adrenergic inhaler only.

Table 43.

37,11%).

Only 36 of 85 patients (42%) in groups A and B and 9 out of 27 patients (33%) in group H who had troublesome wheeze on exercise and an available bronchodilator inhaler ever used this form of therapy before exercise.

Inhaler technique-

All 44 patients using an aerosol bronchodilator in group H demonstrated an efficient inhaler technique and all had been taught this by a doctor. 52 out of 192 patients (27%) in groups A and B using an aerosol bronchodilator inhaler had poor inhaler techniques. Using the classification of Paterson and Crompton (1976), 30(16%) were doubtfully efficient and 22(11%) were totally inefficient. There was little difference between those who had recently attended a hospital clinic (groups A-OPD and B-OPD) and those who attended their general practitioner alone (groups A-GP and B-GP), in whom 14 out of 59 (24%) and 38 out of 133 (29%) had poor techniques respectively.

In groups A and B the following points were noted with regard to inhaler technique-

1) Fewer patients using aerosol corticosteroid or sodium cromoglycate (with or without an aerosol bronchodilator) had poor techniques (19 out of 89, 21%) than those using a bronchodilator as their only aerosol (39 out of 116, 34%) (X^2 3.9 DF1 $p<0.05$).

2) Fewer using an aerosol as their only bronchodilator had poor techniques (23 out of 128, 18%) than those using aerosol and oral bronchodilator therapy combined (29 out of 64, 45%) (X^2 16.2 DF1 $p<0.001$).

3) Fewer patients who had been instructed by their doctor had poor inhaler techniques (30 out of 141, 21%) than the untutored (21

out of 46, 46%) (X^2 10.4 DF1 $p<0.01$).

4) The importance of age can be demonstrated by examining only tutored patients, more patients over 50 years of age had poor techniques (24 out of 74, 32%) than those 50 years and under (6 out of 67, 9%) (X^2 11.6 DF1 $p<0.001$).

The differences in levels of tuition and inhaler techniques between the practice centres are illustrated in table 44, between 63% and 85% of patients had been taught inhaler technique, and the practice with the lowest incidence of inhaler tuition had the lowest incidence of good inhaler technique.

Problems with the use of aerosol inhalers-

Table 45 outlines the main problems in the use of aerosol inhalers in patients in groups A and B. Failure to co-ordinate activation and inhalation was the most common problem (occurring in nearly a third of users).

Alternative inhaler devices-

In groups A and B 13 patients used alternative inhaler devices other than aerosols, including one using a tube spacer inhaler, one a small hand nebuliser, and 11 the dry powder "Rotahaler", 9 of the latter had previously used aerosol inhalers and 7 of these preferred the "Rotahaler" to the aerosol inhaler.

d) ORAL BRONCHODILATORS.

The number of patients using the various types of oral bronchodilators are analysed in table 46. A separate analysis of the over 50 years age group is included in table 47. Both methylxanthines and oral adrenergic drugs were prescribed more frequently in the chronic bronchitics in all age groups. Methylxanthines were usually prescribed in combination with other bronchodilators, in contrast to

Aerosol inhaler technique and the number receiving tuition between the 4 practice centres

	Practice centre			
	1	2	3	4
Number of patients using aerosol inhalers (bronchodilator and prophylactic)	88	25	36	56
Number(%) receiving tuition	55(63%)	19(76%)	29(81%)	47(85%)
		X^2 9.5 DF3 $p<0.05$		
Number(%) with good inhaler technique	55(63%)	22(88%)	23(64%)	47(85%)
		X^2 12.1 DF3 $p<0.05$		

Table 44.

Problems associated with the use of aerosol inhalers.

Number of patients using aerosol inhalers (prophylactic or bronchodilator) in groups A and B	205
Number (%) of patients failing to:	
Shake the cannister	28(14%)
Hold the cannister upright	6(3%)
Coordinate activation and inhalation	56(27%)
Hold breath after activation	45(22%)

Table 45.

The number(%) of patients in groups H, A, and B using the various oral bronchodilator drugs

	Groups		
	H	A	B
Number using bronchodilators	48	172	112
Number(%) using oral bronchodilators	14(29%) :	68(40%) *	81(72%)
Number(%) using methylxanthines	12(25%) :: (1)	28(16%) ** (6)	32(28%) (11)
Number(%) using short acting adrenergic stimulants	0(0%) (0)	28(16%)*** (12)	35(31%) (25)
Number(%) using slow-release $\beta 2$ stimulants	2(4%) (0)	3(2%) (2)	2(2%) (1)
Number(%) using mixed oral drugs (theophylline +ephedrine+barbiturate)	0(0%) (0)	15(9%)**** (6)	15(13%) (10)

: X^2 1.7 DF1 NS
:: X^2 1.9 DF1 NS

* X^2 29.2 DF1 $p<0.001$
** X^2 6.1 DF1 $p<0.05$
*** X^2 8.8 DF1 $p<0.05$
**** X^2 1.0 DF1 NS

The single number in brackets being the number of patients using this drug as their sole bronchodilator.

Table 46.

The use of oral bronchodilators in groups A and B

in patients over 50 years old.

	Groups		
	A		B
Number of patients using bronchodilators	83		105
Number(%) using methylxanthines	19(23%)	*	32(30%)
Number(%) using short acting adrenergic stimulants	12(14%)	**	35(33%)
Number(%) using mixed oral drugs	9(11%)	***	13(12%)

*X^2 1.3 DF1 NS
**X^2 8.8 DF1 $p<0.01$
***X^2 0.1 DF1 NS

Table 47.

A comparison of oral bronchodilator use in groups

A-OPD and A-GP

	Groups	
	A-OPD	A-GP
Number using a bronchodilator	46	126
Number(%) using a methylxanthine	8(17%)	20(16%)
Number(%) using a short acting adrenergic stimulant	6(13%)	22(17%)
Number(%) using a mixed oral drug	4(9%)	11(9%)

Table 48.

the oral adrenergics which were prescribed more often as the sole bronchodilator. In group H methylxanthines were the only commonly used oral bronchodilator therapy (in a quarter of patients) and these were invariably prescribed in combination with inhaled bronchodilators. Group H may not have been typical of drug therapy in hospital clinics, however, as there was little difference in prescribed oral bronchodilator therapy between groups A-OPD and A-GP (see table 48).

As well as there being a significant difference in the number of patients using oral bronchodilator therapy between the practice centres, there were also differences in the use of individual drugs. An analysis of oral bronchodilator usage in asthmatics between the practice centres is included in table 49. In one practice more patients used mixed oral drugs (containing ephedrine and a methylxanthine, with or without a barbiturate) than methylxanthines alone: in another a third of patients using oral therapy used methylxanthines but none used mixed oral drugs.

The use of methylxanthines-

All 12 patients in group H, and 58 out of 60 in groups A and B using methylxanthines took a slow release preparation. All patients in group H took regular therapy in contrast to patients in groups A and B in which 10 (17%) used therapy entirely on demand and a further 7 (12%) who were otherwise regular users took extra doses on demand (all these patients used the slow release preparation). More patients using methylxanthines as their only bronchodilator took therapy on demand (10 out of 17, 58%) than those using methylxanthine combined with another bronchodilator (7 out of 43, 16%) (X^2 10.8 DF1 $p<0.001$). Of 22 asthmatics in group A using adrenergic drugs in combination

The variation in the use of oral bronchodilator therapy in asthmatics (group A) between the pratice centres.

	Practice centre			
	1	2	3	4
Number using bronchodilators	72	25	26	49
Number(%) using methylxanthines	8(11%)	9(36%)	7(27%)	4(8%)
Number(%) using short acting adrenergic stimulants	16(22%)	3(12%)	7(27%)	2(4%)
Number(%) using mixed oral drugs	10(14%)	0(0%)	2(8%)	3(6%)

Table 49.

The number(%) of patients in groups A and B experiencing side effects with oral and inhaled bronchodilator therapy.

	Oral therapy		Inhaled therapy
	n=149		n=203
Number(%) experiencing:			
Tremor	18(12%)	*	12(6%)
Palpitations	14(9%)	**	11(5%)
Gastrointestinal upset	4(3%)		-

*X^2 4.2 DF1 $p<0.05$

**X^2 2.5 DF1 NS

Table 50.

with methylxanthines, 11 did not use associated prophylactic therapy (sodium cromoglycate or inhaled or oral corticosteroids). 7 of these had scores of 2 or 3 for day or night time wheeze.

The dosages of methylxanthines (in mg of theophylline daily or equivalent) prescibed to patients in groups A and B are illustrated in figure 14. In groups A and B only 17% of patients using methylxanthines were prescribed more than 400mg daily (of theophylline or equivalent), whereas this applied to 7 out of 12 patients in group H using this drug.

Oral short acting adrenergic drugs-

No patient in group H used these drugs. In groups A and B they were combined with adrenergic stimulant inhalers in 17 patients (7% of those using a bronchodilator). Significantly more patients using oral short acting adrenergic drugs took regular therapy (46 out of 63, 73%) than those using adrenergic inhalers (44 out of 195, 23%) (X^2 53.4 DF1 $p<0.001$). In a separate analysis of chronic bronchitics 28 out of 35 (80%) patients using oral short acting adrenergic drugs took regular therapy, in contrast to 27 out of 54 (50%) using adrenergic inhalers (X^2 8.1 DF1 $p<0.01$).

The use of slow release oral agents for relief of nocturnal symptoms-

Only 9 out of 39 (23%) patients with grade 3 scores for nocturnal symptoms were prescribed a slow release methylxanthine or adrenergic drug for relief of such symptoms.

e) SIDE EFFECTS OF BRONCHODILATOR THERAPY.

A comparison of the incidence of side effects between inhaled and oral bronchodilator therapy is included in table 50. Oral therapy was associated with approximately twice the incidence of side effects than that occurring with inhaled therapy. The most common adverse

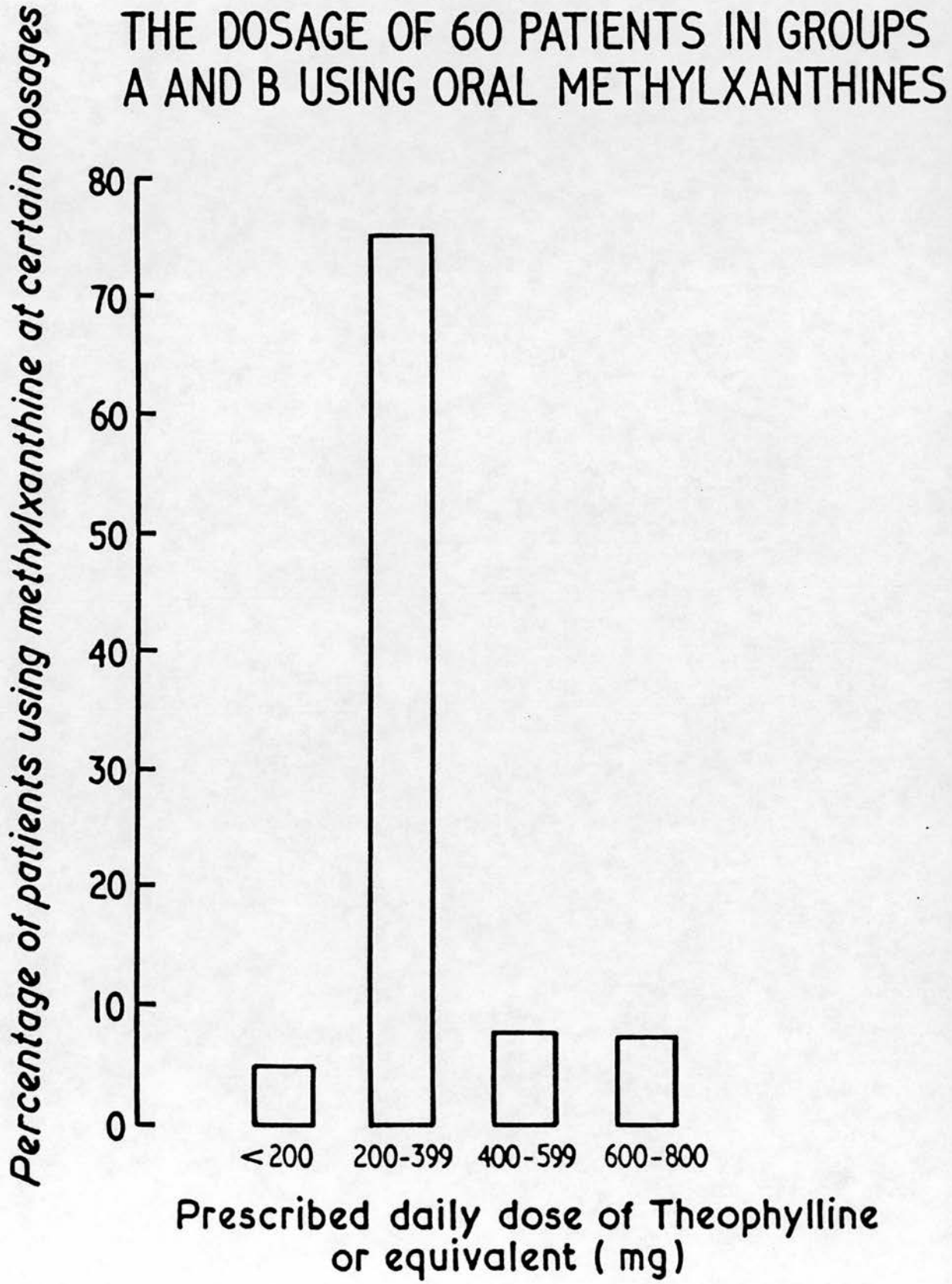

THE DOSAGE OF 60 PATIENTS IN GROUPS A AND B USING ORAL METHYLXANTHINES
Percentage of patients using methylxanthine at certain dosages
80
70
60
50
40
30
20
10
0
<200
200-399
400-599
600-800
Prescribed daily dose of Theophylline or equivalent (mg)

FIGURE 14

effect was tremor.

Patients in groups A and B were also asked what forms of bronchodilator therapy they had had in the past and why such therapy had been discontinued. Twice as many patients had received oral rather than inhaled bronchodilators in the past, and very few patients had tried the dry powder "Rotahaler". Again side effects had been twice as common with oral rather than inhaled therapy. Although few patients admitted to difficulty in the use of aerosol inhalers, nearly a half stopped this form of therapy because of a lack of benefit, suggesting that many may have been using the devices incorrectly. These findings are summarised in table 51.

f) PATIENT PREFERENCE.

Patients were asked which form of bronchodilator delivery they preferred. 27(13%) asthmatics and 23(20%) chronic bronchitics preferred oral therapy, 104(52%) asthmatics and 36(32%) chronic bronchitics preferred inhaled therapy and 70(35%) asthmatics and 54(48%) chronic bronchitics were unable to judge between the two methods of delivery or had no preference. Of the 81 patients using oral therapy alone 66(81%) had never had inhaled therapy in the past.

g) OTHER FORMS OF THERAPY FOR OBSTRUCTIVE AIRWAYS DISEASE.

14(7%) asthmatics and 14(12%) chronic bronchitics used cough suppressants, expectorants, or antihistamines regularly. 30(15%) asthmatics and 38(34%) chronic bronchitics had taken one of these drugs within the previous six months.

The number(%) of patients having received bronchodilator therapy in the past and the reasons for stopping such treatment.

	Aerosol inhalers	Dry-powder inhalers	Oral therapy
	n=45	n=6	n=102
Cause unknown	16(35%)	-	49(48%)
Difficulty in use	7(15%)	3(50%)	-
Lack of benefit	19(42%)	2(33%)	37(36%)
Side effects	3(7%)	1(16%)	18(18%)

Table 51.

f) DISCUSSION

It has been stated that in the care of asthmatics a regular continuity of follow up is essential until self management is satisfactory (Gregg 1983b). Although it is recognised that this study was biased in the selection of those who frequently attended their general practitioners, it was reassuring to see that approximately two thirds of the patients had been seen at least twice in the previous six months by their general practitioner. It might be expected that patients who attended hospital clinics would visit their general practitioner less frequently but this was not the case, and the fact that only a quarter of the patients had attended a hospital clinic in the previous twelve months emphasises the important role of the general practitioner. There are many arguments in favour of maintaining this dominant role (Editorial 1981b), including continuity of care and a more personal approach to management. However, this places the challenge of prescribing suitable and efficient drug therapy firmly with the general practitioner.

Bronchodilators are considered the cornerstone of therapy for obstructive airways disease (Hetzel and Clark 1983) and it was a surprise to find that nearly 1 in 10 of patients in groups A and B used sodium cromoglycate or corticosteroid alone. Over a half of these patients used therapy on demand, suggesting the need for bronchodilators.

The benefits of inhaled rather than oral bronchodilator drugs, including rapidity of action and lack of side effects (Walker et al 1972), are such that a recent editorial (Editorial 1981a) has stated:

"Nowadays, recourse to oral bronchodilator drugs should seldom be necessary."

In this study about 8 out of 10 asthmatics used inhaled bronchodilators, which is a similar proportion to that found in a recent asthma clinic audit (Connolly 1983) and a study of patients dying from asthma (British Thoracic Association 1982). However, oral bronchodilators were also commonly used, especially in the chronic bronchitics. This study has demonstrated that those patients attending a hospital or chest clinic were more likely to use inhaled drugs than those attending their general practitioner alone. The fact that the majority of patients taking oral drugs alone had never been prescribed inhalers and that the majority who were able to choose preferred inhalers, suggests that it is the doctor rather than the patient who is responsible for this prescribing trend.

Patients with chronic bronchitis and chronic asthma often require regular bronchodilator therapy and yet only a half of the former with adrenergic inhalers used these regularly. In contrast 80% of those using oral short acting adrenergic drugs used this therapy regularly. This suggests that the doctor or patient associate oral therapy with regular use but inhaled drugs with symptomatic treatment. There is no obvious rationale for this pattern of prescribing as inhaled adrenergic drugs have similar bronchodilator capacities and lengths of action as their oral counterparts (Walker et al 1972) and the use of regular rather than demand inhaler therapy may improve the control of asthma (Shepherd et al 1981). Patients attending hospital clinics were more likely to take regular inhaled treatment than those attending their general practitioner alone, despite the similarity of PEFR and symptom scores between the two

groups.

Aerosol bronchodilators may be liable to abuse (Pratt 1982). Although this problem may have been underestimated by such patients defaulting from interview, little evidence of this problem was found. It is likely that the use of greater than average doses of inhaled bronchodilators was associated with uncontrolled asthma requiring prophylactic therapy rather than with drug abuse. Underuse of inhaled bronchodilators was more common than overuse, in keeping with a recent study of asthma fatalities (British Thoracic Association 1982). Contrary to previous opinion (Crompton 1983), poor inhaler technique was associated with inhaler underuse rather than overuse. Despite the efficacy of inhaled adrenergic drugs in protecting against exercise induced wheeze (Anderson et al 1976), such therapy was often underused both by the general practitioner and in hospital clinics.

The proportion of patients in general practice receiving tuition was impressively high - in two practices over 80%. The proportion with poor techniques was only slightly worse than that found in a previous hospital study (Paterson and Crompton 1976). However, poor inhaler technique remains a major cause of therapeutic inefficiency. Although improved by tuition this study suggests that older patients are less capable than the younger in this respect. In keeping with previous work (Epstein et al 1979) regular users (those using prophylactic inhalers) were more efficient than those using bronchodilator inhalers. More patients using aerosol and oral bronchodilators in combination had poor inhaler techniques than those using aerosols alone, suggesting that the oral therapy may have been added because of a poor response to the aerosol. Perhaps such

combinations could have been avoided by tuition on inhaler technique. The excellent figures of group H, in which all patients used their aerosol inhalers correctly, may not have been representative of hospital outpatient care as this particular clinic had a rigorous policy of inhaler tuition; indeed there was little difference between groups A-GP and A-OPD in respect of the incidence of poor inhaler technique. Inco-ordination between activation of the aerosol and inhalation is the main problem associated with aerosol inhaler use. Because of this other inhaler devices such as the dry powder "Rotahaler" and tube spacer have been designed (Anonymous 1981); such systems were underused in this study.

There were considerable differences in the prescription of oral bronchodilators between the practices, though in general oral short acting adrenergic drugs were as popular as the methylxanthines. There has been concern in New Zealand about the current trend to use methylxanthines rather than inhaled corticosteroids or sodium cromoglycate when adrenergic drugs have failed to control asthma in adults (Wilson et al 1981). Though the numbers are too small to assess prescription trends, half the asthmatics (group A) in this study using adrenergic drugs and methylxanthines did not use inhaled corticosteroids or sodium cromoglycate and most of these were poorly controlled. The same workers were concerned as to the dangers of using slow release methylxanthines on demand; nearly a third of patients in groups A and B using these drugs took doses on demand, often because a more suitable bronchodilator had not been prescribed.

In the low doses prescribed it is unlikely that many of the patients achieved maximal bronchodilatation from the methylxanthine. Some may have benefitted from higher doses, although low dose regimes

have the advantage of a low incidence of side effects (Weinberger and Hendeles 1983). The role of the methylxanthines in the control of adult asthma remains controversial (Hetzel and Clark 1983). The general practitioners did not measure plasma levels of theophylline and in these circumstances efficient use of these drugs may be difficult. However, there is some evidence that low dose theophylline can be useful in combination with adrenergic drugs (Wolfe et al 1978). Both the slow release methylxanthines and adrenergic drugs have been shown to be of value in protecting against nocturnal wheeze (Milledge and Morris 1979) and in this circumstance were underprescribed.

Despite a lack of objective evidence as to their value (Paterson and Shenfield 1974), mixed oral drugs (containing ephedrine and theophylline with or without a barbiturate) continue to be used (though there was a considerable variation in the use of these drugs between the practice centres). The popularity of mixed oral drugs, despite their relative lack of potency, has been described previously.

Cough suppressants, expectorants and antihistamines are of little value in obstructive airways disease or chronic expectoration. Although such agents were commonly used by patients in this study many are available without prescription and, therefore, their use need not necessarily imply inappropriate prescribing.

CHAPTER 7

PROPHYLACTIC THERAPY

a) The prescription of prophylactic drugs

b) The use of prophylactic inhalers

c) The use of systemic (oral) corticosteroids

d) Discussion

This chapter investigates the use of prophylactic drugs- inhaled and systemic corticosteroids, and sodium cromoglycate.

a) THE PRESCRIPTION OF PROPHYLACTIC DRUGS

Patients were split into 3 grades depending on their PEFRs at interview. The number of patients in each grade and the proportion using prophylactic drugs are illustrated in table 52. There was no significant difference in the proportion of patients using a prophylactic drug between the 3 PEFR grades. Approximately one sixth of the asthmatics (group A) had scores of 2 or 3 for day or night time symptoms but did not use a prophylactic drug; nearly a half of these had PEFRs below 50% of the predicted value. Nearly all patients in group H (43 out of 48, 90%) were prescribed a prophylactic drug.

An analysis of the prophylactic drugs used by patients in groups A and B is shown in table 53. As expected more asthmatics than chronic bronchitics used this form of therapy. Those asthmatics attending a hospital clinic (A-OPD and H) were more likely to use inhaled or oral corticosteroids than those attending their general practitioner alone (A-GP), the reverse was true of sodium cromoglycate (see table 54). Very few patients in either group used ketotifen. In groups A and B sodium cromoglycate was more likely to have been prescribed initially by the patient's general practitioner (in 37 out of 53 cases, 70%) than inhaled corticosteroid, which was more frequently commenced by a hospital doctor (in 53 out of 98 cases, 55%)(X^2 7.9 DF1 $p<0.01$). Of 33 patients using oral corticosteroids, in 24(73%) this was initially commenced by a hospital doctor. The mean ages of patients taking sodium cromoglycate, inhaled corticosteroids and oral corticosteroids were 36.5 years, 53.5 years, and 58.2 years respectively. More patients

The number(%) of asthmatics (group A) and chronic bronchitics (group B) using prophylactic drugs in each of three peak flow grades.

	Grade 1 PEFR >70% predicted	Grade 2 PEFR 50-70% predicted	Grade 3 PEFR <50% predicted	Total
GROUP A	n=104	n=46	n=50	n=200*
Number(%) using prophylaxis	74(71%)	30(65%)	30(60%)	134(68%)
Number(%) without prophylaxis but with a symptom score of 2 or 3	12(12%)	7(15%)	13(26%)	32(16%)
GROUP B	n=21	n=21	n=70	n=112*
Number(%) using prophylaxis	2(10%)	6(29%)	15(21%)	23(21%)

* One asthmatic and one chronic bronchitic unable to provide PEFR recordings.

Table 52.

The number(%) of patients using the different types of prophylactic drugs in groups A and B.

	Groups		
	A	B	Total
	n=201	n=113	n=314
Number(%) using prophylaxis	134(67%)	23(20%)	157(50%)
Number(%) using sodium cromoglycate	50(25%)	3(3%)	53(17%)
Number(%) using inhaled corticosteroids	79(39%)	19(17%)	98(31%)
Number(%) using systemic corticosteroids	29(14%)	4(4%)	33(11%)
Number(%) using ketotifen	3(2%)	-	3(1%)

Table 53.

The number(%) of asthmatics using the various prophylactic drugs in groups H, A-OPD, and A-GP.

	Groups		
	H	A-OPD	A-GP
	n=48	n=51	n=150
Number(%) using prophylaxis	43(90%)	39(76%)	95(63%)
	X^2 13.1 DF2 p<0.01		
Number(%) using sodium cromoglycate	2(4%)	5(10%)	45(30%)
Number(%) using inhaled corticosteroid	40(83%) *	29(57%) **	50(33%)
Number(%) using systemic corticosteroid	19(40%)	22(43%)	7(5%)

* X^2 3.05 DF2 NS
** X^2 34.9 DF2 p<0.001

Table 54.

using sodium cromoglycate had high PEFRs (>70% predicted) than those using inhaled corticosteroids (see figure 15), though the range of symptom scores was similar between patients using these two drugs (see figure 16). As expected more patients using oral corticosteroids had severe disease with higher symptom scores and lower PEFRs.

There were considerable differences in the use of these drugs in the asthmatics between the practice centres (see table 55). The practice with the greatest proportion using sodium cromoglycate (centre 3) had the fewest using inhaled corticosteroid, and the reverse trend was seen in practice centre 4. These differences in prescribing could not be explained by variation in the severity of disease in the patients between the practices (as seen by the proportion of patients with PEFRs below 50% predicted).

In groups A and B 27 patients used combinations of sodium cromoglycate, inhaled and oral corticosteroids, including 19 taking the latter two drugs, and 8 taking the former two drugs. In group H only the combination of inhaled and oral corticosteroids was used (by 18 of 48 patients). Of 98 patients who used inhaled corticosteroids 12(12%) used the dry powder form of delivery. 53 patients used sodium cromoglycate, of whom 31(58%) used the compound of sodium cromoglycate and isoprenaline, 18(34%) the plain formulation, and 4(8%) the aerosol preparation.

b) THE USE AND PRESCRIPTION OF PROPHYLACTIC INHALERS

56(39%) of those patients using prophylactic inhalers were poorly compliant (poor compliance was defined as the omission of at least one treatment daily from the prescribed dose). The dose most likely to be omitted was the lunch time treatment of a TID or QID regime.

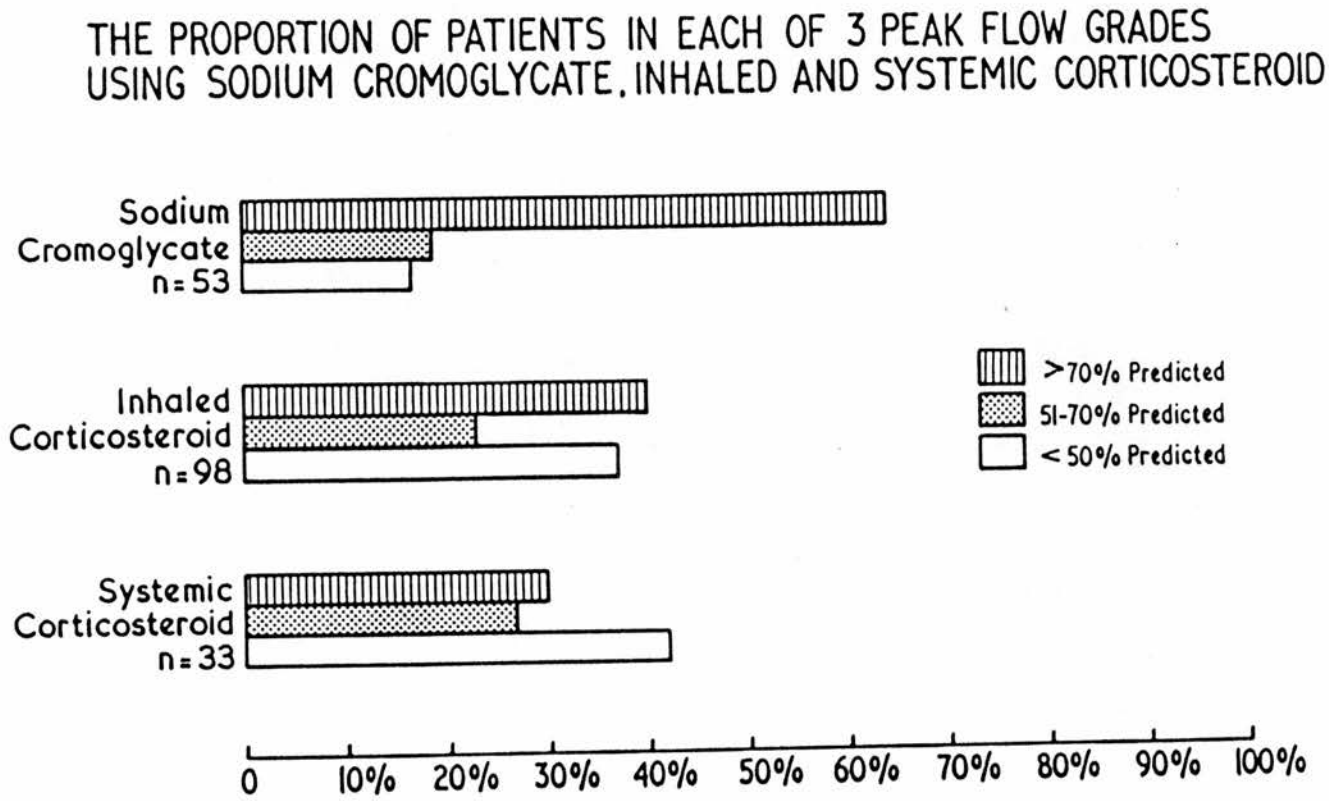

THE PROPORTION OF PATIENTS IN EACH OF 3 PEAK FLOW GRADES
USING SODIUM CROMOGLYCATE, INHALED AND SYSTEMIC CORTICOSTEROID
Sodium
Cromoglycate
n=53
Inhaled
Corticosteroid
n=98
Systemic
Corticosteroid
n=33
>70% Predicted
51-70% Predicted
< 50% Predicted
0
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%

FIGURE 15

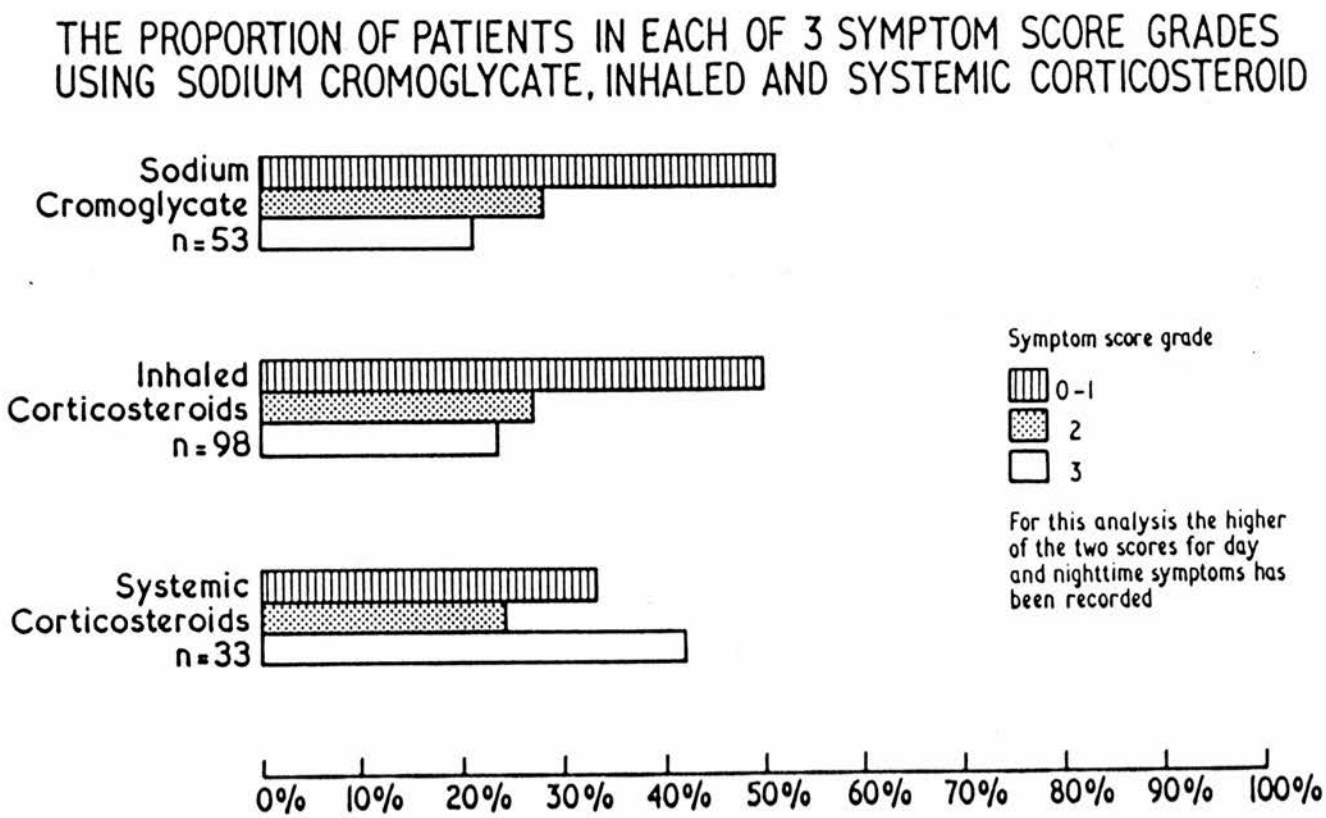

THE PROPORTION OF PATIENTS IN EACH OF 3 SYMPTOM SCORE GRADES USING SODIUM CROMOGLYCATE, INHALED AND SYSTEMIC CORTICOSTEROID
Sodium Cromoglycate n=53
Inhaled Corticosteroids n=98
Systemic Corticosteroids n=33
Symptom score grade
0-1
2
3
For this analysis the higher of the two scores for day and nighttime symptoms has been recorded
0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

FIGURE 16

The number(%) of asthmatics using the various prophylactic drugs between the 4 practice centres.

	Practice Centre			
	1	2	3	4
	n=84	n=30	n=33	n=54
Number(%) using prophylaxis	53(63%)	18(60%)	23(69%)	40(74%)
		X^2 2.9 DF3 NS		
Number(%) using sodium cromoglycate	19(23%)	8(27%)	13(39%)	10(18%)
Number(%) using inhaled corticosteroid	29(34%)	11(36%)	7(21%)	32(59%)
Number(%) using systemic corticosteroid	16(19%)	3(10%)	7(21%)	3(6%)
		X^2 17.2 DF6 $p<0.01$		
Number(%) with a PEFR <50% predicted	14(17%)	14(47%)	9(27%)	11(20%)

Table 55.

Of these 56 poor compliers, 16 (11% of prophylactic inhaler users) took treatment entirely on demand, 10 took some regular treatment but also extra doses on demand, the remaining 30 took only regular treatment but omitted doses. A further 27 patients took regular therapy at full dosage but took extra doses on demand depending on symptoms. More patients using sodium cromoglycate compound took treatment on demand (either totally or partially) (19 out of 31, 61%) than those using sodium cromoglycate plain (8 out of 22, 36%)or inhaled corticosteroid (26 out of 98, 27%)(X^2 12.3 DF2 $p<0.01$).

Inhaler technique was classed as efficient, doubtfully efficient and inefficient (Paterson and Crompton 1976). 12(13%) patients were found to be doubtfully efficient and 7(8%) inefficient.

A summary of the incidence of poor compliance, demand usage and poor inhaler technique and the proportion of these patients who had scores of 2 or 3 for day or night time symptoms is included in figure 17. In group H there were significantly fewer poor compliers (9 out of 42, 21%) than in groups A and B (56 out of 142, 39%) (X^2 4.6 DF1 $p<0.05$); very few (2 out of 42, 5%) used their prophylactic inhalers entirely on demand. However, recent hospital attenders in groups A and B (A-OPD and B-OPD) were similar in their incidence of poor compliance (13 out of 39, 33%) as those who attended their general practitioners alone (groups A-GP and B-GP) (43 out of 103, 42%) (X^2 0.8 DF1 NS).

Patient knowledge of prophylaxis-

All patients using a prophylactic drug were asked if this protected them against wheeze (or shortness of breath), or treated these symptoms once they were present. 84 out of 142 (59%) chose the

The number (%) of patients in groups A and B exhibiting various errors in the use of prophylactic inhalers.

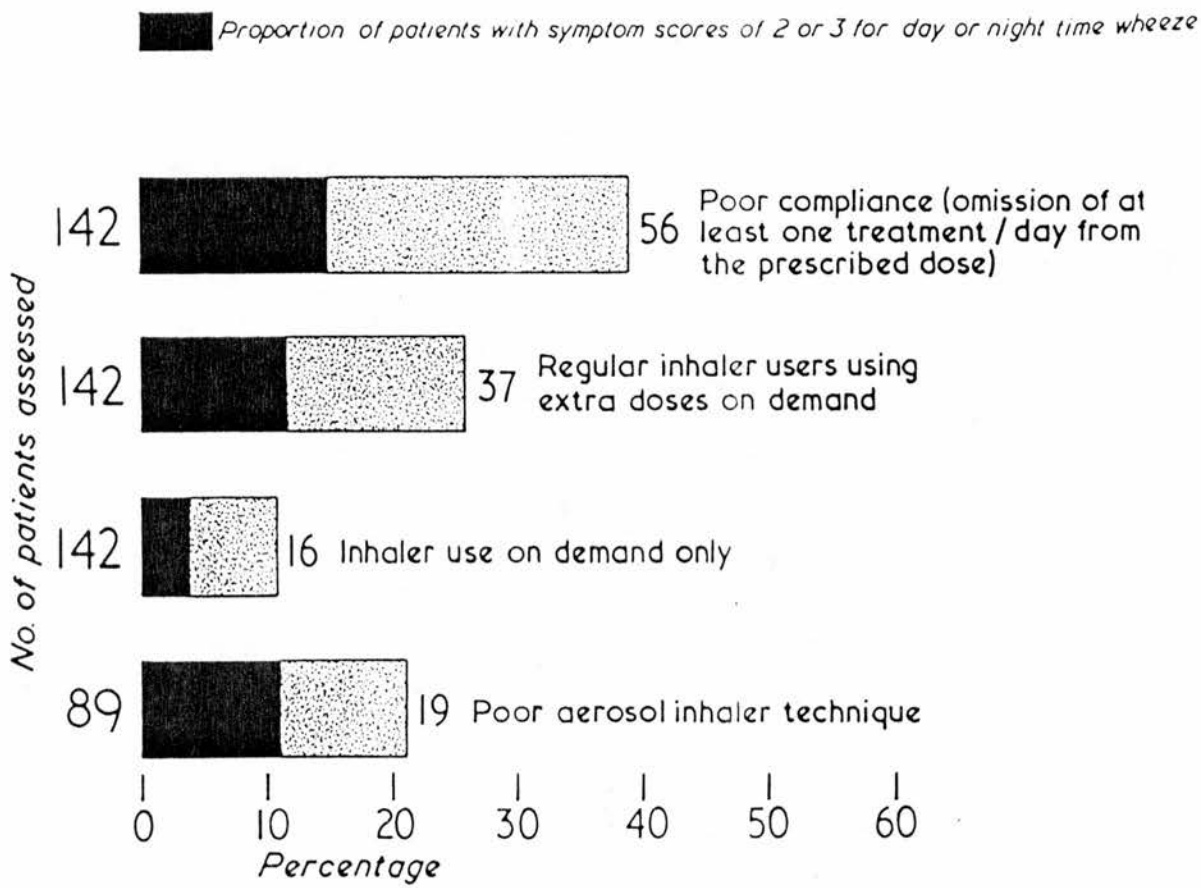


FIGURE 17

first correct response. The proportion of patients who realised the protective nature of the drugs varied insignificantly between the practices as did the number of poor compliers (see table 56). Patients who used their inhalers regularly but always took less than the prescribed dose had a good level of knowledge (24 out of 30, 80% gave correct responses). These patients differed from those who used their inhalers on demand (either totally or partially) in whom there was a poor level of knowledge (20 out of 53, 38% gave correct responses) (X^2 13.7 DF1, $p<0.001$).

Although more compliant, patients in group H had a similar level of knowledge as those in groups A and B with 26 out of 42 (62%) realising the prophylactic nature of the drugs.

Problems with the prescription of prophylactic inhalers-

In groups A and B 17 compliant patients (12% of inhaler users) were prescribed below standard doses (<400 mcg of beclomethasone diproprionate or <4 capsules of sodium cromoglycate daily) and 28(20%) standard doses, despite both groups having scores of 2 or 3 for day or night time symptoms, suggesting that additional therapy may have been beneficial. The prescribed doses of inhaled prophylaxis are illustrated in figure 18. The highest prescribed dose of inhaled corticosteroid in groups A and B was 12 puffs (600mcg beclomethasone diproprionate) daily. In group H only 1 out of 42 patients was prescribed less than standard dosage and 17 out of 40 using inhaled corticosteroid were prescribed at least 800 mcg daily of beclomethasone diproprionate.

Combining the problems of prophylactic inhaler use and underprescribing 74 out of 142 (52%) of patients in groups A and B either had a poor inhaler technique, omitted at least one treatment

The number(%) of patients in groups A and B using prophylactic inhalers who understood the protective nature of the drug and the number(%) who were non-compliant - the variation between the practice centres.

	Practice Centre				
	1	2	3	4	Total
	n=53	n=24	n=21	n=44	n=142
Number(%) understanding the protective nature of the drug	31(58%)	10(42%)	11(52%)	32(73%)	84(59%)
		X^2 6.8 DF3 NS			
Number(%) who were non-compliant	19(36%)	6(25%)	11(52%)	20(45%)	56(39%)
		X^2 4.5 DF3 NS			

Table 56.

THE PRESCRIBED DOSAGES OF INHALED CORTICOSTEROID AND SODIUM CROMOGLYCATE IN PATIENTS IN GROUPS A AND B

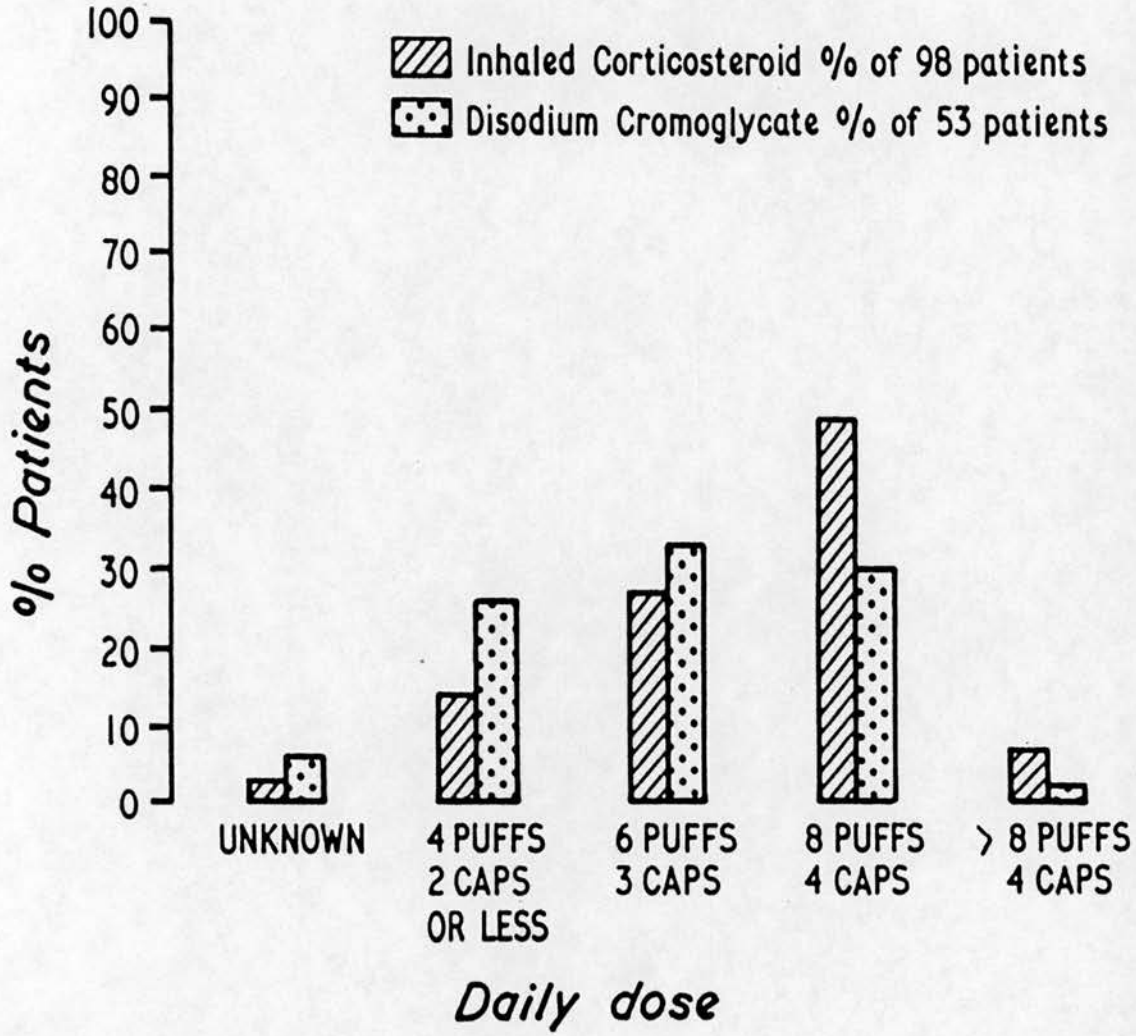


Figure 18

daily from the prescribed regime, or were fully compliant but were prescribed a below standard dose despite a score of 2 or 3 for day or night time symptoms. Fewer patients in group H took inefficient therapy (9 out of 42, 21%) than those in groups A and B (74 out of 142, 52%) (X^2 12.3 DF1 $p<0.001$). However when comparing groups A-OPD and B-OPD with those in A-GP and B-GP a similar proportion were found to take inefficient therapy (22 out of 39, 56% and 52 out of 103, 50% respectively). Of the 74 patients in groups A and B using inefficient therapy 43(58%) had scores of 2 or 3 for day or night time symptoms.

Side effects of prophylactic inhalers-

The incidence of sore throat, hoarseness, and previous treatment for oral thrush in patients using inhaled corticosteroids is analysed in table 57. More patients in group H using this drug reported side effects than those in groups A and B, with a fifth of patients in group H having had previous treatment for oral thrush.

25 of the 49 patients (51%) using the spinhaler for sodium cromoglycate complained of coughing after inhalation. A similar proportion using the plain preparation complained of coughing (9 out of 18, 50%) as those using the compound with added isoprenaline (15 out of 31, 48%).

c) THE USE OF SYSTEMIC (ORAL) CORTICOSTEROIDS

The number of patients who were taking, or who had previously taken systemic corticosteroids for their chest complaint in groups A, B, and H are shown in table 58. In all but one patient (who used A.C.T.H. and therefore indirect therapy) this was oral treatment. Over a half of the patients in group A either took or had taken systemic corticosteroids in the past, whereas this applied to less than a fifth of patients in group B. Nearly all the asthmatics in group H were

The side effects reported by patients using inhaled corticosteroids in groups A+B, and H.

	Groups	
	A+B	H
	n=98	n=40
Number(%) reporting sore throat	5(5%)	10(25%)
	X^2 11.6 DF1 p<0.001	
Number(%) reporting hoarseness	10(10%)	9(22%)
	X^2 3.6 DF1 NS	
Number(%) having had previous treatment for oral thrush	1(1%)	8(20%)
	X^2 16.8 DF1 p<0.001	

Table 57.

The number(%) of patients who were taking or had previously taken systemic corticosteroid in groups A, B, and H.

	Groups		
	H	A	B
	n=48	n=201	n=113
Number(%) currently taking systemic corticosteroids	19(40%)	29(15%)	4(4%)
Number(%) who had previously taken systemic corticosteroids:-			
As a long course (>6 weeks)	2(4%)	21(10%)	3(3%)
As a short course (<6weeks)	23(48%)	67(33%)	14(12%)
Total number of patients who had taken or were taking systemic corticosteroids	44(92%)	117(58%)	21(18%)

Table 58.

taking or had taken systemic corticosteroids in the past. The dosages and lengths of time on treatment of the 33 patients in groups A and B, and 19 in group H who were currently taking this drug are analysed in table 59. The majority used less than 10mg of prednisolone or equivalent daily and most patients in groups A and B had been taking the drug for at least 5 years.

The medical surveillance of patients using regular systemic corticosteroid in groups A and B-

The attendances of 33 patients using regular systemic corticosteroids in groups A and B are illustrated in table 60. The majority (73%) had attended a hospital outpatient clinic within the previous 12 months and only one patient had had no recent medical surveillance either in a hospital clinic or by the general practitioner.

The use of inhaled corticosteroid with the oral drug-

14 of 33(42%) patients in groups A and B did not use inhaled corticosteroid with the oral drug, and 10(30%) had never had inhaled corticosteroid at any time. Patients attending their general practitioner alone (A-GP and B-GP) were more likely to use oral corticosteroid without inhaled corticosteroid (6 out of 9, 66%) than those who also attended a hospital clinic (A-OPD and B-OPD) (8 out of 24,33%). 2 out of the former group used prednisolone as their only therapy for airways obstruction, with no available bronchodilator. In group H only 1 out of 19 patients using oral corticosteroid did not also use the inhaled form.

The use of "booster" doses by patients on regular systemic corticosteroids-

23(70%) patients in groups A and B and 12(63%) in group H had

The dosage (of prednisolone or equivalent) and length of time on treatment of patients in groups A+B, and H, currently using systemic corticosteroid.

	Groups	
	A+B	H
	n=33	n=19
DOSAGE*		
<5mg	7(21%)	6(32%)
5-10mg	23(70%)	13(68%)
>10mg	2(9%)	-
LENGTH OF TIME ON TREATMENT		
<1 month	3(9%)	1(5%)
<1 year	4(12%)	3(15%)
1-5 years	5(15%)	11(58%)
>5 years	21(64%)	4(21%)

* One patient in group A+B using A.C.T.H.

Table 59.

The frequency of attendance by 33 patients in groups A and B using oral corticosteroids in a specialist clinic and at the general practice surgery.

No. of specialist clinic attendances in the previous 12 months	No. of attendances at the general practice surgery in the previous 6 months				
	Never	Once	2-5	>5	Total
Never	1	2	3	3	9
Once	0	1	12	5	18
2-5	0	1	4	0	5
>5	0	0	1	0	1
Total	1	4	20	8	33

Table 60.

used raised "booster" courses for troublesome symptoms. The majority usually did so without a doctor's supervision and the increases taken were usually small (<20mg of prednisolone daily or equivalent) and were usually for periods of less than one week. A summary of "booster" dosage is included in table 61.

Side effects of systemic corticosteroids-

Of 52 patients in groups A, B, and H taking regular systemic corticosteroids 29(56%) had noticed weight gain, 23(44%) facial changes, 15(29%) indigestion, 4(8%) had symptoms associated with documented osteoporosis, 4(8%) complained of bruising easily and 1 was a diabetic. A further 24 patients in groups A and B and 2 in H had had a prolonged course of oral corticosteroids (>6 weeks) in the past. The incidence of side effects in these patients was similar.

The use of short courses of systemic corticosteroids-

Of patients not taking regular systemic corticosteroids, 67(33%) in group A, 14(12%) in group B, and 23(48%) in group H had had a previous short course of the drug. The details of dosage, frequency, and outcome of these courses and whether they were usually prescribed by their own general practitioner or a hospital doctor is included in table 62. More patients in group H were normally prescribed these courses by a hospital doctor than those in groups A and B. Threequarters of the patients were prescribed a cumulative dose of at least 100mg of prednisolone (or equivalent) and approximately a half received the drug for at least a week; in only a seventh of patients did the symptoms relapse after the course. Although patients in groups A, B, and H appeared to have been prescribed similar courses, when the patients were split into two groups- firstly those in whom the courses were normally prescribed by

The use of "booster" doses by patients taking regular systemic corticosteroids.

	Groups		
	A+B	H	Total
Number of patients using systemic corticosteroid	33	19	52
Number(%) who had taken booster courses	23(70%)	12(63%)	35(67%)
Of those who had taken booster courses of systemic corticosteroid:			
A) The number(%) who usually did so without medical supervision	14(61%)	8(66%)	22(63%)
B) The number(%) who usually took an increase in daily dose of:			
≤20mg	16(70%)	5(42%)	21(60%)
>20mg	7(30%)	7(58%)	14(40%)
of prednisolone or equivalent			
C) The number(%) who usually took the course for			
≤1week	14(61%)	6(50%)	20(57%)
>1week	9(39%)	6(50%)	15(43%)
D) The number(%) who usually took the course at a frequency of			
1/year	8(35%)	3(25%)	11(31%)
2-6/year	14(61%)	9(75%)	23(66%)
>6/year	1(4%)	0(0%)	1(3%)

Table 61.

The prescription of short courses of systemic corticosteroids- the dosage, length of course, and frequency of courses prescribed to 81 patients in groups A and B, and 23 in group H.

	Groups	
	A+B	H
Number of patients who had previously taken a short (<6wks) course of oral corticosteroids	81	23
Number(%) of patients who had taken:		
No	38(47%)	3(13%)
1	29(36%)	9(39%)
2-6	14(17%)	10(43%)
>6	0(0%)	1(4%)
courses in the previous 12 months		
Number(%) of patients who were usually prescribed a cumulative dose of:		
<50mg	2(2%)	0(0%)
50-100mg	15(18%)	3(13%)
>100mg	60(74%)	17(74%)*
of prednisolone or equivalent		
Number of patients who were usually prescribed a course for		
<3 days	2(2%)	0(0%)
3-7 days	30(37%)	10(43%)
>1 week	48(59%)	10(43%)*
Number(%) of patients in whom the symptoms relapsed after a course		
often	11(14%)	3(13%)
rarely	4(5%)	4(17%)
never	66(81%)	16(69%)
Number(%) of patients in whom the course was normally prescribed by:		
the GP	58(72%)	7(30%)
a hospital doctor	23(28%)	16(70%)

*data not available in 3 patients

Table 62

the general practitioner, and secondly those in whom the courses were normally prescribed by a hospital doctor, more of the latter were prescribed a cumulative dose of at least 100mg of prednisolone (35 out of 36, 97%) than the former (42 out of 61,69%) (X^2 11.1 DF1 $p<0.01$)(in 7 patients the dosage was unknown).

d) DISCUSSION

Although two thirds of the asthmatics seen in general practice were using prophylactic agents, it is likely that nearly half the remainder would have benefitted from this group of drugs, as many had frequent symptoms and low PEFRs. It was interesting to see that the use of prophylactic drugs appeared to be independent of the PEFR grade at interview. This could be due to the poor correlation between respiratory function and symptoms in asthma (Rubinfield and Pain 1976) or the fluctuation of airways obstruction in this condition. In the younger asthmatic the identification and treatment of persistent airways obstruction may be important if permanent disability is to be avoided (McNicol and Williams 1976).

The type of prophylactic drugs used in those patients who attended their general practitioners alone and those who also attended a hospital clinic differed markedly. Some specialist clinics have a policy of never discharging patients using long term oral corticosteroids, and this may explain the high proportion of patients in groups A-OPD and H using these drugs. Patients using sodium cromoglycate were younger and tended to have higher PEFRs than those using inhaled corticosteroids. This suggests that those asthmatics using the former had less severe disease, though it is noticeable that their symptom scores were similar to those using inhaled corticosteroid. There was a trend for the general practitioner rather

than a hospital specialist to prescribe sodium cromoglycate, with the reverse trend being applicable to inhaled corticosteroid. It was noticeable, however, that there were marked differences in the use of these two agents between the practices.

Although up to 70% of adult asthmatics may respond to sodium cromoglycate (Northern General Hospital Brompton Hospital and MRC collaberative trial 1976), relapse after a period of good control is not uncommon (Godfrey 1975). In general inhaled corticosteroid is a more potent suppressing drug in adult asthma, and it is likely that many of the patients who were symptomatic on sodium cromoglycate would have achieved better control using inhaled corticosteroid. Sodium cromoglycate has little steroid sparing effect (Toogood et al 1981) and it is unlikely that the 8 patients in group A using the combination of corticosteroid and sodium cromoglycate were deriving benefit from the latter. Despite the observed popularity of sodium cromoglycate compound rather than the plain preparation there is little evidence to support its value (Brompton Hospital MRC collaborative trial 1972) and the frequent use of this drug on demand supports the theory that the immediate relief obtained from the isoprenaline in the compound may lead the patient to be confused as to the role of the drug (Gregg 1982).

Poor compliance was the major problem with the use of prophylactic inhalers and its incidence of 39% was similar to that found in a recent hospital outpatient study (James et al 1982). Two types of poor compliance were identified: firstly those patients who took regular treatment but always at below the prescribed dose, and secondly those patients who used the drug on demand; of course in some patients these two errors co-existed. The first type of poor

compliance, unlike the second, was not related to a poor level of knowledge of the prophylactic function of the drug. The practical implications of this is that while patients may be taught not to use therapy on demand, many would continue to regularly omit doses. These findings are substantiated by a study of antihypertensive therapy in which a careful education programme failed to improve the level of poor compliance (Sackett et al 1975). It may be considered that many patients were poor compliers because, as in hypertension, they felt well. However, nearly a half of this group had troublesome symptoms. There is now evidence that twice daily dose regimes using higher individual doses are as efficacious as the four times daily regime for inhaled corticosteroid (Munch et al 1982). Though the effect of twice daily dose regimes on compliance requires further study, there seems little doubt that such regimes would be more convenient. Patients attending hospital clinics were more compliant than those attending their general practitioners alone, but this was not associated with an increased knowledge of the function of the drugs. This improved compliance may have been associated with the stimulus of a more severe underlying disease, though it has been noted previously that symptoms need not stimulate good compliance.

Although the majority of patients can be controlled on standard doses of inhaled prophylactic drugs some may benefit from larger doses of sodium cromoglycate (Bernstein 1981) and inhaled corticosteroid (Toogood et al 1977). Certainly it is difficult to defend the prescription of below standard doses in symptomatic patients. In contrast to groups A and B nearly all patients attending hospital clinics (group H) were prescribed at least standard dosage (400mcg beclomethasone diproprionate or equivalent).

When combining the problems of prophylactic inhaler use over half the patients in groups A and B took inefficient therapy. Although the corresponding figure in group H was less, this group may not have been representative of the impact of hospital clinics on the care of patients with airways obstruction, as groups A-OPD and B-OPD were similar in terms of the incidence of inefficient therapy to groups A-GP and B-GP.

The incidence of oral thrush in patients using inhaled corticosteroids has been variably reported between 4.5% when based on a single examination (Willey et al 1976), to 77% for cumulative incidence (Brompton Hospital MRC collaberative trial 1974). Obviously the difference in these figures may be in part due to the different criteria used for diagnosing oral thrush. However, there seems little doubt that the incidence of oral thrush is dose related (Milne and Crompton 1974) and this may explain the higher incidence of oral thrush in group H in whom higher doses of inhaled corticosteroids were prescribed. Although hoarseness and sore throat are the usual symptoms of oral thrush, the former may occur without thrush (Willey et al 1976) and may be associated with the local effects of corticosteroid on the musculature on the larynx.

It is well known that the dry powder of sodium cromoglycate in the spinhaler may cause throat irritation, cough and occasionally wheeze. Because of the latter complaint a compound of isoprenaline with cromoglycate was developed. Though a half of the patients in this study had noted coughing with the spinhaler there was no difference in the incidence between those patients using cromoglycate plain and those using the compound.

Nearly a third of patients using oral corticosteroids in

groups A and B were supervised by their general practitioners alone, although in the majority of cases it had been commenced initially by a hospital doctor. The level of medical surveillance of this group was impressive with only one patient having had no recent general practitioner or hospital clinic attendance.

The use of inhaled rather than oral corticosteroids where feasible is now established practice and 400mcg of beclomethasone diproprionate and 7.5mg of prednisolone are roughly equivalent (British Thoracic and Tuberculosis Association 1975). It was a surprise, therefore, to find that 42% of patients using oral corticosteroids were not also using the inhaled form. Though this may have been the policy of the local specialist clinic, it is noticeable that the use of oral corticosteroids without the inhaled drug occurred more frequently in those patients attending their general practitioner alone. In groups A and B it is likely that substantial reductions in the use of oral corticosteroids could have been made by an increased use of the inhaled drug. This is important because of the high incidence of side effects which can be associated with the long term use of these drugs. Despite the moderate dosages used by patients in this study, at least a half had noticed weight gain and facial changes and nearly a tenth had symptoms of underlying osteoporosis. The side effects are dose related, and therefore attempts to keep doses to a minimum are wise.

In order to maximise control, patients using oral corticosteroids should be well educated, and discretion should be entrusted to them as to dose changes. The majority of patients in this study took booster doses without medical supervision, illustrating a large degree of self management. Though the dose

increases were usually only modest in most cases they were successful in alleviating symptoms and as such are difficult to criticise.

Short courses of oral corticosteroids are prescribed for two main reasons, firstly to treat exacerbations of symptoms and secondly as a trial to elucidate whether a patient with chronic airways obstruction is "corticosteroid responsive". The majority of chronic bronchitics seen in this survey had severe symptoms, and yet only 1 in 10 had had a previous course of oral corticosteroids. Such "trial" treatment could be considered to have been underused in this group of patients. As previously discussed some of the patients had medical conditions which may have made the general practitioner reluctant to prescribe the drug, however, the possible benefits often outweigh the risks involved. This study has demonstrated a group of patients with typical symptoms of chronic bronchitis with a good response to oral corticosteroids, whose control may have beeen greatly improved by the use of regular inhaled corticosteroids. There has been concern that general practitioners do not prescribe large enough doses of corticosteroids in short courses. Evidence from this study, however, suggests that this is uncommon, with the majority (69%) being prescribed a cumulative dose of at least 100mg of prednisolone. Nevertheless patients receiving courses from a hospital clinic were more likely to be prescribed higher doses.

CHAPTER 8

CONCLUSIONS.

a) Part 1

b) Part 2

Part 1

The first part of this study was concerned with the diagnosis of patients with airways obstruction. General practitioners have been criticised in the past for misdiagnosing patients with asthma, labelling them instead as having chronic bronchitis or emphysema (Seaton 1978). There is an impression that the airways obstruction in chronic bronchitis is often considered to be irreversible, and therefore, is undertreated. Usually only the symptomatic history is used in making a diagnosis, however, it is unclear how reliable the symptomatic history is in identifying patients with variable (or reversible) airways obstruction. Gregg has demonstrated how simple reversibility studies may be undertaken in general practice using peak flow meters to identify patients with reversible airways obstruction (Gregg 1964). Such studies may be of great value in the diagnosis and assessment of patients with obstructive airways disease but in practice are frequently omitted. The value of undertaking reversibility studies using bronchodilators and corticosteroids was examined.

In general practice two main diagnoses were used- asthma and chronic bronchitis. In the absence of any quantifiable abnormality, such as in diabetes mellitus or thyrotoxicosis, it was impossible to either prove or disprove a diagnosis of asthma. It was not the aim of the study, therefore, to criticise the general practitioners' diagnoses, but to examine the validity of the separation of patients into these two diagnostic categories. Because of the selection methods used in the study, patients with "simple" chronic bronchitis (chronic cough and expectoration only) were not included, and only those with symptomatic airways obstruction were seen. Such cases were

more likely to have been mistaken for the asthmatic patient.

Two aspects of the patient's condition were examined: firstly the symptomatic history, and secondly, the reversibility of the patient's airways obstruction to drug therapy. The relationship between these two features was assessed. Finally, the drug therapy of those patients with demonstrable airways reversibility was examined. After consideration of the results of this part of the study some simple guidelines for general practitioners dealing with patients with obstructive airways disease are suggested.

The following conclusions were made:-

1) The symptoms that were most valuable in separating patients diagnosed as having asthma from those having chronic bronchitis were, in order:- a) an absence of chronic cough and expectoration, b) a history of hayfever, c) a history of exercise induced wheeze, d) a history of episodic symptoms, e) an early onset of symptoms, f) an absence of cigarette smoking.

General practitioners should enquire into the presence of these symptoms when considering the diagnosis of asthma.

2) Patients could be separated into the two groups, asthma and chronic bronchitis, using the symptomatic history. However, there was considerable overlap between the groups, such that in clinical practice approximately a third of the patients would be difficult to diagnose accurately using the symptomatic history. The cause of this overlapping of symptoms in asthma and chronic bronchitis has been discussed earlier in the thesis. Simply it may be due to the fact that in some patients asthma (variable airways obstruction) and chronic bronchitis (chronic expectoration due to atmospheric pollution or smoking) co-exist.

The general practitioner should be aware that for some patients the symptomatic history is not a reliable basis for diagnosis.

3) There was little difference in the degree of bronchodilator reversibility between those patients diagnosed by their general practitioners as having asthma and those having chronic bronchitis. Only very large responses were specific for a symptomatic diagnosis of asthma. An analysis of the symptomatic history in patients with good and poor bronchodilator reversibility emphasised the poor correlation between the two.

Corticosteroid reversibility is often considered to be synonymous with asthma. In this study there were no characteristic symptoms with which one could predict good corticosteroid reversibility and some patients with symptoms typical of asthma had a poor response to oral corticosteroids whereas some with symptoms typical of chronic bronchitis had a good response. In conclusion there are ranges of reversibility to bronchodilators and corticosteroids in patients with asthma and chronic bronchitis and these correlate poorly with their symptoms.

The general practitioner should realize that it is impossible to reliably predict a patient's response to bronchodilators or corticosteroids using the symptomatic history.

4) About a third of patients who were given a trial of high dose oral corticosteroids responded well to this form of therapy and nearly all these patients had moderate or severe symptoms. Less than a quarter of the responsive patients used inhaled corticosteroids and almost all who did take this drug used below standard doses. All the responsive patients could be considered to have been undertreated.

The study has demonstrated, therefore, the value of undertaking trials of high dose oral corticosteroids, to identify those patients who would benefit from prophylaxis with this drug (preferably in the inhaled form). These can easily and safely be used in general practice. Bronchodilator reversibility studies are a useful simple way of demonstrating variable airways obstruction and the value of this form of therapy to the patient. They may be insensitive, however, and a poor response should not necessarily militate against the use of a bronchodilator.

General practitioners should be aware that patients with demonstrable airways reversibility are undertreated, because of an inadequate assessment of their reversibility to corticosteroids. As responsiveness to this drug cannot reliably be predicted from the symptomatic history, trials of this therapy should be undertaken more readily.

b) PART 2

The second part of the study examined the type and efficacy of therapy used by patients in general practice and compared those seen by their general practitioners alone with those who also attended specialist clinics. When criticising drug therapy allowances have to be made for individual prescribing habits. As in most other conditions, there is more than one correct way to treat obstructive airways disease. In assessing therapy, therefore, care is required not to be prejudiced in favour of one's own therapeutic practice. On the other hand individual therapy can be compared with standard therapeutic practices that are advised by most modern reference works, that are undertaken in most asthma clinics, and that are taught in our medical schools. By examining care in several general

practices it was hoped that the general prescribing trend was emphasised rather than that pertaining to individuals.

Audits of care in asthma clinics have been undertaken previously, but how representative of the care of asthma in this country are they? Obviously they are dominated by the clinical practice of the clinic involved and this study has shown that only a quarter of asthmatics requiring treatment are likely to attend such a clinic. Unfortunately there are difficulties in comparing disease severity and efficiency of disease control between patient groups. For instance one group with severe underlying disease but with optimal treatment may have similar symptoms and PEFRs as a group with mild underlying disease which is badly treated. Bearing this in mind, apart from having slightly higher PEFRs and fewer previous hospital admissions, asthmatics who attended their general practitioners alone had a similar severity of symptoms as those attending specialist clinics. Thus the bulk of the care of asthma occurs in general practice and this applies to all grades of severity. In the case of chronic bronchitis the dominance of general practice care is even greater. It may be considered that attendance at a specialist clinic would replace general practice care, but this was not so as there were similar general practitioner attendance rates in those patients who attended specialist clinics and those who did not.

Audits in asthma clinics may be a false indicator of the impact of specialist care on the patient's management and, therefore, two groups were assessed: firstly a consecutive series of asthmatics attending a hospital clinic (in which the patient was interviewed at the clinic), and secondly those patients who were seen in general practice but had also attended a specialist clinic within the

previous 12 months. This study has shown that although the first group usually used more efficient therapy than those seen by their general practitioner alone, this did not always apply to the second group.

What specific conclusions can be drawn form the detailed analysis of drug therapy used in general practice?

1) Approximately a tenth of the patients used corticosteroid or sodium cromoglycate alone without an available bronchodilator. In most cases this was inappropriate.

2) Patients attending specialist clinics were more likely to use inhaled bronchodilators than those attending their general practitioner. The majority of patients using oral bronchodilators alone had never used inhalers, but of those who could choose between the two methods of delivery the majority preferred inhalers. This suggests that it is the doctor rather than the patient who is responsible for this prescribing trend of oral bronchodilators.

3) Chronic bronchitics, unlike asthmatics, were more likely to be prescribed oral rather than inhaled bronchodilators. This may have been because general practitioners associated oral therapy with regular treatment and inhaled therapy with treatment on demand. This is illogical, as inhaled therapy can be used regularly and would have benefitted many asthmatics and chronic bronchitics in this study. When comparing patients with a similar severity of symptoms, those attending specialist clinics were much more likely to use regular inhaled therapy than those attending their general practitioner alone.

4) Very few patients were found to be using large doses of inhaled bronchodilators, and this was more likely to be associated with

uncontrolled asthma requiring prophylactic treatment rather than inhaler abuse. Underuse of inhalers was more common and was often associated with poor inhaler technique.

5) Poor inhaler technique was a major problem in the use of aerosol inhalers. Although improved by tuition older patients were less capable than the younger. Patients seen in the specialist clinic were much better in this respect, however, this did not apply to those seen in general practice who had also recently attended a specialist clinic.

6) There were marked differences between the practices in the prescription of oral bronchodilators. Mixed oral drugs (containing theophylline, and ephedrine with or without a barbiturate) continue to be used, though only infrequently in most practices.

7) Slow release methylxanthines were usually prescribed by the general practitioners in low dosage. It is likely that some of the patients would have benefitted from larger doses. Despite being unsuitable for demand usage over a quarter of patients used the drug in this fashion, often because a more suitable bronchodilator was not available.

8) Approximately a sixth of asthmatics with moderate or severe symptoms did not use inhaled or oral corticosteroids or sodium cromoglycate. A half of this group also had PEFRs below 60% predicted. This represents underuse of these agents.

9) Unlike inhaled corticosteroids, sodium cromoglycate was more likely to be initiated by the general practitioner than a hospital doctor. Relatively few patients attending specialist clinics used sodium cromoglycate. Half the patients using this drug had moderate or severe symptoms and may have been helped by increased doses or a

change to inhaled corticosteroids.

10) Poor compliance was a major problem in the use of inhaled prophylactic drugs and occurred in 4 in 10 patients. Although less common in patients attending specialist clinics, these differences were not marked. Two main types were identified: firstly the use of the drugs on demand, which was associated with a poor understanding of the function of the drugs, and secondly the omission of drugs every day in an otherwise regular user. This study emphasises the importance of non-compliance as many of these patients had troublesome symptoms. These results implied that education would not be entirely successful in eradicating the problem. Less frequent daily dose regimes might be valuable in improving compliance.

11) Some compliant patients were prescribed below standard doses of inhaled corticosteroid or sodium cromoglycate despite being symptomatic. Patients attending specialist clinics were usually prescribed higher doses of inhaled corticosteroid.

12) Combining the problem of poor compliance, poor inhaler technique, and underprescription half of the patients using inhaled corticosteroids or sodium cromoglycate were using inefficient therapy. Though patients seen in a specialist clinic were more likely to be using efficient therapy, this did not apply to those seen in general practice but who had recently attended a specialist clinic.

13) Nearly a third of patients using oral corticosteroids did not use concomitant inhaled corticosteroids. This was more likely to occur in those patients attending their general practitioners alone. A substantial reduction in the use of oral corticosteroids may have been possible with the increased use of inhaled corticosteroids.

14) Despite the high incidence of incapacity in the chronic

bronchitics only about a tenth had previously had a short course of oral corticosteroids. It is likely that this form of treatment both for assessment and treatment of exacerbations was underused. Patients receiving short courses of oral corticosteroids from hospital doctors tended to be prescribed higher doses for longer periods than those from the general practitioners.

This study has illustrated considerable differences in the management of obstructive airways disease between practices. Single practice audits, therefore, do not accurately reflect general standards of care in the community. Although it is an improvement to study several practices, it is a fault of this study that these were not chosen at random. Unfortunately this problem would be difficult to overcome. It is interesting that audits in asthma clinics may also fail to give a true reflection of their impact on patient management.

Many therapeutic problems have been highlighted in this summary. How can they be avoided? Obviously awareness of their occurrence is the first step. Some of the problems could be eradicated by repeated instruction of the patient. However, some of the fault lies with inappropriate prescribing and the main message from this study is the undertreatment of patients both with the appropriate drugs and their dosages. What is the cause of this undertreatment? It is possible that some patients were undertreated because of the use of the disease label- chronic bronchitis, however, many asthmatics were also undertreated. It is likely that this was caused by an anxiety about the safety of asthma therapy, and ignorance concerning the indications and optimal use of the various therapies. Much work is required, therefore in demonstrating the efficiency and safety of modern therapy to fellow practitioners and

patients alike.

DECLARATION OF ORIGINALITY

I declare that the work reported in this thesis was originated and performed by me, with the exception of assistance in computing detailed in the acknowledgments. I also declare that this thesis was composed entirely by myself.

PUBLICATIONS ARISING FROM WORK IN THIS THESIS

Wardman A.G., Binns V., Clayden A.D. Cooke N.J.

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APPENDIX

Enquiries to:

Extension:

Our ref:

Your ref:

Date: Date as Postmark

Dear Sir or Madam

I am a doctor currently working with your general practice, with the aim of assessing the treatment and control of wheezy chest conditions. At present you are receiving treatment for your chest. I would be most grateful, therefore, if you could help me by attending the surgery at the time and date shown below for a short interview (approx. 20 minutes), in which we will discuss how troublesome your symptoms are and what treatment you take. Should your symptoms be severe it may be useful to give you a short course of tablets to see if your wheeze responds.

Unless you have especially troublesome symptoms please do not take treatment in the four hours before the interview.

Time ---------- Date ----------

If this time is not suitable I would be grateful if you could contact ---------- at the surgery and a more convenient appointment will be made for you.

In anticipation of your kind co-operation.

Yours faithfully

Andrew G Wardman MB., MRCP.

General Practitioner

APPENDIX I

APPENDIX II

TREATMENT OF WHEEZE PATIENT ASSESSMENT PROFORMA

Patient Number: ☐☐☐

Name ---------- DOB ----------

Address ----------

---------- Tel no: ----------

GP: ---------- Occupation ----------

Husband's occupation: ----------

Date of Interview ----------

1. SEX

1	2
M	F

☐

2. AGE

1	2	3	4
18-30	30-50	51-70	70+

☐

3. SOCIAL CLASS

1	2	3	4	5
I	II	III	IV	V

☐

4. ARE YOU TROUBLED WITH WHEEZE

1	2	3
YES	NO	DON'T KNOW

☐

5. IF YES FOR HOW LONG

0	1	2	3	4
NO TROUBLE	<1 Yr	1-5 Yrs.	5-10 Yrs.	>10 Yrs.

☐

6. IS IT

1	2	3
Continuous wheezing most days out of the year	Episodic wheezy attacks with symptom free periods	NEITHER

☐

7. IS IT

1	2	3
Seasonal	Perennial (most months)	NEITHER

☐

8. IF SEASONAL, IS IT

0	1	2	3
NOT SEASONAL	SUMMER	WINTER	NEITHER

☐

5a. HOW OLD WERE YOU WHEN YOUR WHEEZE/SHORTNESS OF BREATH BECAME NOTICEABLE?

1	2	3
<20 Yr	20-40	>40 Yr

☐

PATIENT ASSESSMENT PROFORMA

9. DO YOU ASSOCIATE YOUR WHEEZE

a) with occupation - Present

1	2	3
YES	NO	DON'T KNOW

10. Past

1	2	3
YES	NO	DON'T KNOW

If YES what occupation

---

11. b) Hobbies

1	2	3
YES	NO	DON'T KNOW

If YES what hobbies

---

12. c) Contact with Animals

1	2	3
YES	NO	DON'T KNOW

13. d) URTI

1	2	3
YES	NO	DON'T KNOW

14. Do/Did you suffer from hayfever

1	2	3
YES	NO	DON'T KNOW

15. Do/Did you have eczema

1	2	3
YES	NO	DON'T KNOW

16. Have you a family history of hayfever and or asthma

1	2	3
YES	NO	DON'T KNOW

17. What time of day is your wheezing worse

0	1	2	3	4
NO CHANGE	MORNING	DAY	EVENING	NIGHT

18. Do you have cough and sputum most days for at least three months out of the year in the past two years

1	2	3
YES	NO	DON'T KNOW

19. Do/Did you smoke regularly

1	2	3	4
YES	NO	Ex < 5 years	Ex > 5 years

19A What form of tobacco do/did you smoke mostly

0	1	2	3
NONE	CIGARETTE	PIPE	CIGAR

20. How many if a cigarette smoker?

(cigarettes/day)

0	1	2	3
NIL	<10	10-20	>20

21. Did/does smoking affect your wheeze?

0	1	2	3	4
None smoker	Better	Worse	no change	don't know

22. Have you been warned about smoking by your doctor?

0	1	2	3
None smoker	YES	NO	Don't know

23. If you have stopped smoking, why?

0	1	2	3
Not applic-able	Own volition because of wheeze	Own volition other reasons	Medical Warning

24. Have you attended hospital/Chest Clinic with your wheeze.

a) INPATIENT

1	2
YES	NO

25. b) OUT-PATIENT

1	2
YES	NO

26. Frequency:

a) INPATIENT (total)

0	1	2	3
NIL	<2	2-5	>5

27. b) OUT-PATIENT (past year)

0	1	2	3
NIL	<2	2-5	>5

28. What chest condition do you have?

1	2	3	4	5
Asthma	Chronic Bronchitis	Emphysema	C.O.A.D.	Don't know

29. G.P. Diagnosis:

1	2	3	4	5
Asthma	Chronic Bronchitis	Emphysema	C.O.A.D.	Don't know

30. Hospital Diagnosis:

1	2	3	4	5
Asthma	Chronic Bronchitis	Emphysema	C.O.A.D.	Not Recorded

ASSESSMENT OF WHEEZE CONTROL

31. Are you satisfied with your wheeze control

1	2
YES	NO

32. Is your condition:

1	2	3
Static	Deteriorating	Improving

33. How often have you seen uour GP with wheeze in the past six months?

0	1	2	3
NIL	<2	2-5	>5

34. Have you required emergency housecalls by your G.P. in the past six months for wheeze?

0	1	2	3
NIL	<2	2-5	>5

35. Have you required injections by your G.P. in past 6 months?

1	2
YES	NO

36. How many weeks off School/work have you had in the past year?

0	1	2	3
NIL	<2	2-5	>5

37. If episodic how many episodes of wheeze lasting more than 1 hour have you had in the past month?

0	1	2	3	4
NIL	<5	5-20	20+	NOT EPISODIC

38. If you have morning tightness how long does it normally last?

0	1	2	3	4
NIL	<½ hr	½-1 hr	1-2 hrs	2 hrs+

39. Do you have more severe wheeze on exercise (continuing after exercise has ceased)?

1	2
YES	NO

40. Does this regularly interfere with your activity?

1	2
YES	NO

41. Do you regularly participate in sport?

1	2
YES	NO

Which Sport? _____

DRUG THERAPY

42. Which drugs do you take for wheeze: _____ ☐

43. _____ ☐

44. _____ ☐

45. _____ ☐

46. _____ ☐

47. _____ ☐

48. _____ ☐

49. _____ ☐

50. Which drugs have you taken in the past for wheeze: _____ ☐

51. _____ ☐

52. _____ ☐

53. _____ ☐

54. _____ ☐

55. _____ ☐

56. _____ ☐

57. _____ ☐

58. Do you take any of the following regularly:

Beta Blockers

1	2
YES	NO

☐

59. Asprin

1	2
YES	NO

☐

60. Antibiotics

1	2
YES	NO

☐

61. Cough suppressants, expectorants, antihistamines

1	2
YES	NO

☐

62. Which method of therapy do you prefer:

1	2	3	4
ORAL	AEROSOL INHALER	DRY POWDER INHALER	DON'T KNOW

☐

INHALER USE

63. Are you using an aerosol inhaler?

1	2
YES	NO

64. Were you shown how to use the inhaler

a) by your G.P.

1	2
YES	NO

65. b) by pharmacist

1	2
YES	NO

66. Do you think you use the inhaler correctly

1	2	3
YES	NO	DON'T KNOW

67. Inhaler technique score:

1	2	3
EFFICIENT	DOUBTFULLY EFFICIENT	INEFFICIENT

68. Inhaler technique - cannister shaken

1	2
YES	NO

69. cannister held upright

1	2
YES	NO

70. co-ordination of activation and inspiration

1	2
YES	NO

71. breath held after inhalation

1	2
YES	NO

72. WAS:

1	2
Mouth held open	Pursed round inhaler

BRONCHODILATORS

Inhalers (Aerosol)

73. Are (were you) using a bronchodilator aerosol inhaler?

1	2	3
YES	NO	IN PAST

PRESENT

74. DRUG:-

75. Is it used regularly without regard to wheeze?

1	2
YES	NO

76. Is it used on demand?

1	2
YES	NO

77. Average Dosage - Puffs/day:

1	2	3	4	5
<2	2-8	9-16	17-24	>24

78. Do you use the drug before exercise?

1	2
YES	NO

79. Is it beneficial before exercizing?

1	2	3
YES	NO	NOT USED

80. How long does relief from the inhaler last?

0	1	2	3	4
NO RELIEF	<1 hour	1-2 hours	2-4 hours	DON'T KNOW

81. How long does an inhaler normally last?

1	2	3	4
<2 weeks	2-4 weeks	4-8 weeks	>8 weeks

82. Have you noticed side effects:

Tremor

1	2
YES	NO

83. Palpitations

1	2
YES	NO

84. Other:

1	2
YES	NO

If yes, please specify _____

_____

If inhaled bronchodilators used in the past, why was the drug stopped?

85. DRUG:-

86. Cause unknown

1	2
YES	NO

87. Difficulty in patient use

1	2
YES	NO

88. Lack of Benefit

1	2
YES	NO

89. Side Effects:

Palpitations

1	2
YES	NO

90. Tremor

1	2
YES	NO

91. Other

1	2
YES	NO

If yes, please specify: _____

_____

92. Worry about danger

1	2
YES	NO

93. Other cause

1	2
YES	NO

INHALED BRONCHODILATOR (DRY POWDER)

94. Do you use Salbutamol Rotacaps

1	2	3
YES	NO	IN PAST

95. Dose of capsule

1	2
200 ug	400 ug

96. Is it used regularly without regard to wheeze

1	2
YES	NO

97. Is it used on demand

1	2
YES	NO

98. Average dose per day:

1	2	3	4
400µg	400-1600µg	1600-3200µg	>3200µg

99. Do you use the drug before exercise

1	2
YES	NO

100. Is it beneficial before exercising

1	2
YES	NO

101. How long does relief from the inhaler normally last?

0	1	2	3	4
NO RELIEF	< 1 hr	1-2 hrs	2-4 hrs	4 hrs

102. Have you noticed side effects:

Tremor or palpitations

1	2
YES	NO

103. Coughing

1	2
YES	NO

104. Other

1	2
YES	NO

If yes, please specify: ----------

---

105. Have you tried an aerosol inhaler?

1	2
YES	NO

☐

106. Do you prefer the dry powder delivery technique?

1	2	3
YES	NO	DON'T KNOW

☐

107. Used in the past - why was drug stopped?

1	2	3	4	5
Cause Unknown	Difficulty in patient use	Lack of benefit	Side Effects	Other Causes

☐

Which Side Effect: _____

_____

ORAL BRONCHODILATORS

108. Are you using (have you used) oral bronchodilators?

1	2	3
YES PRESENT	NO	IN PAST

☐

PRESENT

109. DRUG ☐☐☐☐☐☐

110. Is it used regularly without regard to wheeze?

1	2
YES	NO

☐☐☐

111. Is it used on demand?

1	2
YES	NO

☐☐☐

112. Is it?

1	2	3
RECOMMENDED DOSE	BELOW RECOMMENDED DOSE	ABOVE RECOMMENDED DOSE

☐☐☐

Which Dose? _____

113. Do you use the drug before exercising

1	2
YES	NO

☐☐☐

114. Is it beneficial?

1	2	3	4
YES	NO	DON'T KNOW	NOT USED

☐☐☐

115. How long does relief last with tablets?

0	1	2	3	4
NO RELIEF	< 2 hrs	2-4 hrs	4-8 hrs	> 8 hrs

☐☐☐

116. If used at bedtime does it stop nocturnal wheeze?

0	1	2	3
NO NOCTURNAL WHEEZE	VERY BENEFICIAL	MODERATELY BENEFICIAL	POOR

☐☐☐

117. Have you noticed side effects?

Tremor

1	2
YES	NO

118. Palpitations

1	2
YES	NO

119. G.I. upset

1	2
YES	NO

120. OTHER

1	2
YES	NO

If yes, please specify ----------

PAST

121. Why was the drug stopped?

DRUG:

122. Cause unknown

1	2
YES	NO

123. Lack of benefit

1	2
YES	NO

124. Side Effects:

Tremor

1	2
YES	NO

125. Palpitations

1	2
YES	NO

126. G.I. upset

1	2
YES	NO

127. Worry about danger

1	2
YES	NO

128. Other cause

1	2
YES	NO

Please specify ----------

129. Have you ever tried an inhaler?

1	2	3
YES PRESENT	YES (PAST)	NO

SUPPOSITORIES

130. Have you used/are you using Aminophylline suppositories?

1	2	3
YES PRESENT	NO	IN PAST

☐

131. Do/did you use them?

1	2	3
REGULARLY	IRREGULARLY	NOT USED

☐

132. Do/did you find them beneficial?

1	2	3
YES	NO	NOT USED

☐

133. Did you experience any rectal irritation?

1	2	3
YES	NO	NOT USED

☐

PROPHYLAXIS - INTAL

134. Are you using (have you used) Intal (Sodium Cromoglycate)

1	2	3
YES PRESENT	NO	IN PAST

PRESENT

DRUG:

135. Do you take the drug regularly without regard to wheeze?

1	2
YES	NO

136. Dose:

1	2	3
< 2 caps (4 puffs per day)	2-4 caps (4-8 puffs per day)	> 4 caps (8 puffs per day)

137. Are doses missed?

1	2	3	4
RARELY	ONCE PER WEEK	ONCE PER DAY	AT LEAST TWICE A DAY

138. Is it used on demand for wheezy attacks?

1	2
YES	NO

139. Is it helpful?

1	2
YES	NO

140. Do you use Intal before exercise

1	2
YES	NO

141. Is it beneficial?

1	2
YES	NO

142. Does Intal:

1	2
Protect against wheeze	Treat wheeze once it is present

143. Were you shown how to use the spinhaler:

1	2	3
YES	NO	TAKING AEROSOL

144. Do you find the spinhaler technique usage

1	2	3	4
Easier than aerosol	Harder than aerosol	Same as aerosol	DON'T KNOW

145. Have you noticed side effects - coughing after Intal?

1	2
YES	NO

146. Was the drug commenced

1	2
by G.P.	by Hospital doctor

PAST

DRUG:

Why was Intal stopped?

147. Cause unknown

1	2
YES	NO

148. Lack of benefit

1	2
YES	NO

149. Side effects coughing

1	2
YES	NO

150. side effects other

1	2
YES	NO

151. Worried about danger

1	2
YES	NO

152. Other cause

1	2
YES	NO

INHALED CORTICOSTEROIDS

153. Are you using (have you used) a Becotide/Bextasol inhaler?

1	2	3
YES	NO	IN PAST

154. PRESENT

Do you use the drug regularly without regard to wheeze?

1	2
YES	NO

155. Dose:

1	2	3	4
<2 Puffs per day	2-4 Puffs per day	4-8 Puffs per day	8-16 Puffs per day

156. Are doses missed?

1	2	3	4
RARELY	ONCE PER WEEK	ONCE PER DAY	AT LEAST TWICE PER DAY

157. Is it used on demand for wheezy attacks?

1	2
YES	NO

158. Is it helpful?

1	2
YES	NO

159. Do you use the inhaler before exercise?

1	2
YES	NO

160. Is it beneficial?

1	2
YES	NO

161. Does Becotide/Bextasol?

1	2
PROTECT AGAINST WHEEZE	TREAT WHEEZE ONCE IT IS PRESENT

162. How long does an inhaler last?

1	2	3	4
<2 Weeks	2-4 Weeks	4-8 Weeks	>8 Weeks

163. Have you had hoarseness with the inhaler?

1	2
YES	NO

164. Have you had sore throat with inhaler?

1	2
YES	NO

☐

165. Have you required treatment for oral thrush?

1	2
YES	NO

☐

166. Was the drug commenced?

1	2
BY G.P.	BY HOSPITAL DOCTOR

☐

167. <u>PAST</u>

Why was Becotide stopped?

1	2	3	4	5
Cause unknown	Lack of benefit	Side effects- hoarseness, sore throat, thrush.	Worried about danger	Other causes

☐

ORAL STEROIDS

168. Are you taking (have you taken) oral steroids for wheeze?

1	2	3
YES	NO	IN PAST

PRESENT

169. Was the drug first prescribed by?

1	2
G.P.	HOSPITAL DOCTOR

170. How long have you been taking steriods?

1	2	3	4	5
<1 month	1-6 months	6 months - 1 year	1 year -5 years	>5 years

171. What dose of steroids do you take (Prednisolone equivalent)

1	2	3	4
<5mgs	5-10mgs	10-15mgs	>15mgs

172. Do you alter your steroid dose with respect to your wheeze?

1	2
YES	NO

173. Is this on your doctors recommendation?

1	2	3	4
RARELY	USUALLY	ALWAYS	NEVER ALTER

174. By how much do you increase your steroid dose for an exacerbation of wheeze (in Prednisolone equivalent)?

1	2	3	4	5
<10mgs	10-20mgs	20-40mgs	>40mgs	never alter

175. How long do you normally take the raised dose?

1	2	3	4	5
<3 days	3-7 days	1-2 wks	>2 wks	never alter

176. When lowering the dose to baseline treatment do you use a reducing schedule?

1	2	3
YES	NO	NEVER ALTER

177. Does your wheeze relapse after reducing the dose?

1	2	3
OFTEN	RARELY	NEVER ALTER

178. How often do you take raised courses (per year)

1	2	3	4	5
<2	2-6	6-12	>12	never alter

179. Have you noticed any of the following since steroid therapy?

Weight gain

1	2	3
YES	NO	DON'T KNOW

180. G.I. effect

1	2	3
YES	NO	DON'T KNOW

181. Changes in facial appearance

1	2	3
YES	NO	DON'T KNOW

182. If you are not on a steriod inhaler have you been

1	2	3
ON STEROID INHALER	YES	NO

183. Were the steroids commenced

1	2
BY G.P.	BY HOSPITAL DOCTOR

184. PAST (short course)

Was the drug used in one or more short courses lasting less than 6 weeks.

1	2	3
YES	NO	DON'T KNOW

185. <u>IF YES</u> - How many courses have been given in the past 1 year?

1	2	3	4
<2	2-6	>6	Course given over 1 year.

186. How much steroid is normally given in total (Prednisolone equivalent)

1	2	3	4	5
<50 mgs	50-100 mgs	100-300 mgs	>300 mgs	don't know

187. When stopping the drug is a reducing schedule used?

1	2	3
Reducing schedule over several days	Stopped quickly over 24 hrs.	DON'T KNOW

188. How long has the course lasted usually?

1	2	3	4
<3 Days	3-7 Days	1-2 weeks	>2 weeks

189. Does your wheeze relapse after the course?

1	2	3
Often	rarely	never

190. Who usually prescribes the course?

1	2
G.P.	Hospital Doctor

191. Is the course ever commenced by the patient from his or her own stock without the G.P.'s knowledge?

1	2
YES	NO

192. <u>PAST</u> (<u>Long course</u>)

Was the drug ever used in a course lasting longer than 6 weeks?

1	2
YES	NO

193. What daily dose was used? (Prednisolone equivalent)

1	2	3	4
<5mg	5-10mg	10-15mg	>15mg

194. Why was the drug stopped?

Cause unknown

1	2
YES	NO

195. Lack of benefit

1	2
YES	NO

196. Side effects:

Weight gain

1	2
YES	NO

197. G.I. effects

1	2
YES	NO

198. Facial changes

1	2
YES	NO

199. Worry about dangers

1	2
YES	NO

200. Other cause

1	2
YES	NO

201. KETOTIFEN

Are you taking (have you taken) Ketotifen

1	2	3
YES	NO	IN PAST

202. PRESENT

Do you use the drug regularly without regard to wheeze?

1	2
YES	NO

203. Dose per day:

1	2	3
<2mgs	2-4mgs	>4mgs.

204. Are doses missed?

1	2	3	4
Rarely	once per week	once per day	at least twice a day

205. Is it used on demand for wheezy attacks?

1	2
YES	NO

206. Is it helpful?

1	2
YES	NO

207. Does Ketotifen:

1	2
Protect against wheeze	Treat wheeze once it is present

208. Have you noticed any side effects?

1	2
YES	NO

What _____

209. Did you experience drowsiness?

1	2
YES	NO

210. PAST

Why was the drug stopped?

1	2	3	4
Cause unknown	lack of benefit	side effects	Other cause

State side effect _____

211. ANTIBIOTICS

How many courses of antibiotics have you had for your wheeze in the past year?

1	2	3	4
NIL	<2	2-4	>4

212. DESENSITISATION

Have you had desensitisation for your chest?

1	2
YES	NO

213. EXPECTORANTS & ANTIHISTAMINES

Do you take the above for wheeze or have you taken it in the past six months

1	2
YES	NO

214. Please grade your wheeze control by marking the line below at an appropriate site:

NOT AT ALL TROUBLESOME ——— EXTREMELY TROUBLESOME

215. Please grade your wheeze as an average in the month before interview:

0 No wheeze - able to do all activities

1 Slight wheeze - able to do most activities

2 Moderate wheeze - activities limited regularly by frequent wheeze

3 Severe wheeze - activities constantly curtailed by wheeze

216. 0 No nocturnal wheeze

1 Slight nocturnal wheeze (woken occasionally - less than once per week)

2 Moderate nocturnal wheeze (woken frequently - 1-3 times per week - with wheeze)

3 Severe nocturnal wheeze (very frequently woken - more than 3 times a week - with wheeze

CONSULTATION 1		CONSULTATION 2 (Post Steroid)
	PEFR (best of 3)	
	Predicted PEFR	
	% Predicted	
	PEFR post Salbutamol if below <80% predicted	
	% Reversal (from predicted)	
	Prednisolone reversibility if PEFR <60% predicted, or grade 3 assessment	

217. % predicted PEFR:

1	2	3	4	5	6
>90%	81-90	71-80	61-70	51-60	41-50
7	8				
31-40	21-30				

218. Salbutamol reversibility done -

1	2
YES	NO

219. % reversal

1	2	3	4
<10%	10-20%	21-30%	>30%

220. Prednisolone reversibility done -

1	2
YES	NO

221. Prednisolone reversibility:

1	2	3	4
<10%	10-20%	21-30%	>30%

219A. Bronchodilator reversibility:

DRUG THERAPY

Inhaled Bronchodilators

A) Aerosols

1 Salbutamol (Ventolin)
2 Terbutaline (Bricanyl)
3 Terbutaline (Spacer) (Bricanyl)
4 Orciprenaline (Alupent)
5 Fenoterol (Berotec)
6 Reproterol (Bronchodil)
7 Rimiterol (Pulmadil)
8 Rimiterol Auto (Pulmadil Auto)
9 Isoetharine (Bronchodilator)
10 Isoprenaline (Isoautohaler, Medihaler Iso (Duo) PIB, Brontosil, Aleudrin)
11 Adrenaline (Asma-Vydrin, Brovon, Silbe, Medihaler-Epi)
12 Ipratropium Bromide (Atrovent)

B) Dry Powder Inhaled Bronchodilators

13 Salbutamol Rotacaps

Oral Bronchodilators

14 Salbutamol (Syrup or Tablet)
15 Salbutamol Spandet
16 Terbutaline (S or T)
17 Terbutaline SA
18 Orciprenaline (S or T)
19 Reproterol (T)
20 Isoetharine T (Numotac)
21 Isoprenaline (Aleudrin)
22 Ephedrine ± Theophylline ± Barbiturate (Amesec, Asmapax, CAM, Expansyl Spansule, Nethaprine, Tedral, Franol)
23 Theophyllines (Choledyl, Labophylline, Monotheamin, Nuelin, Silbephylline, Theodrox).
24 Theophylline (sustained release) (Nuelin SA, Phyllocontin Continuing, Slo-Phyllin, Theo-Dur, Theograd, Uniphyllin, Unicontin)

Suppositories

25 Aminophylline (Theosol)

Prophylaxis

Intal
26 Intal (Sodium Cromoglycate) Plain Spincap
27 Intal (" ") Compound Spincap
28 Intal (" ") Aerosol

Inhaled Steroids

29 Beclomethasone Diproprionate (Becotide)
Betamethasone Valerate (Bextasol)

Oral/Parenteral Steroids (ACTH)

30 Prednisolone, Dexamethasone
Betamethasone, Triamcinolone
31 ACTH

Ketotifen

32 Ketotifen

Expectorants and Antihistamines

33 Phensedyl, Actifen, Benylin, etc.

RESPIRATORY FUNCTION CHART

PREDICTED NORMALS	FEV_1		FVC		PEFR	

REVERSIBILITY BEFORE AND AFTER BRONCHODILATOR AEROSOL						
DATE						
	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER
FEV_1						
FVC						

SURNAME

FIRST NAMES

UNIT NUMBER

PEAK FLOW RECORDINGS																											
1st BLOW																											
2nd BLOW																											
3rd BLOW																											
DATE																											
TIME	BD	8a.m.	8p.m.	8a.m.	8p.m.	8a.m.	8p.m.	8a.m.	8p.m.	8a.m.	8p.m.	8a.m.	8p.m.	8a.m.	8p.m.	8a.m.	8p.m.	8a.m.	8p.m.	8a.m.	8p.m.	8a.m.	8p.m.	8a.m.	8p.m.	8a.m.	8p.m.	8a.m.
	TDS	8a.m.	2p.m.	8p.m.	8a.m.	2p.m.	8p.m.	8a.m.	2p.m.	8p.m.	8a.m.	2p.m.	8p.m.	8a.m.	2p.m.	8p.m.	8a.m.	2p.m.	8p.m.	8a.m.	2p.m.	8p.m.	8a.m.	2p.m.	8p.m.	8a.m.	2p.m.	8p.m.